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Title

Geographic and socioeconomic differences in uptake of Pap test and mammography in Italy: results from the National Health Interview Survey

Short title

Factors associated with Pap test and mammography uptake

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Abstract

Objective: The Italian National Health Service (NHS) instituted cervical and breast cancer screening programmes in 1999; the local health authorities have a mandate to implement these screening programmes by inviting all women aged 25-64 for a Pap test every three years (or for an HPV test every five years) and women aged 50-69 for a mammography every two years (with the exception of two regions, which start screening at age 45). However, the implementation of screening programmes throughout the country is still incomplete. We thus analysed data both from the Italian National Health Interview Survey (NHIS) conducted by the National Institute of Statistics (ISTAT) in 2012-2013 and from the Italian National Centre for Screening Monitoring to measure Pap test and mammography uptake and their socioeconomic determinants.

Methods: A national representative random sample of 32,831 women aged 25-64 and of 16,459 women aged 50-69 was interviewed. Logistic multilevel models were used to estimate the effect of socioeconomic variables and behavioural factors on screening uptake. Data on screening invitation coverage at the regional level were used as ecological covariates.

Results: Total three-year Pap test and two-year mammography uptake was 62.1% and 56.4%, respectively; screening programmes accounted for 1/3 and 1/2 of total test uptake, respectively. Strong geographical differences were observed. Uptake was associated with high educational levels, healthy behaviours, being a former smoker, and being Italian vs. foreign national. Differences in uptake between Italian regions were mostly explained by the invitation coverage to screening programmes.

Conclusions: The uptake of both screening programmes in Italy is still under acceptable levels. Screening programme implementation has the potential to reduce the health inequalities gap between regions but only if uptake increases.

Keywords: Pap test, mammography, socioeconomic, immigrants, geographic, Italy

Strengths and limitations of this study

- The large amount of information derived from NHIS survey allowed to investigate thoroughly inequities in screening uptake in Italy for the first time.
- The joint use of two data sources enabled to estimate the impact of screening programmes on uptake in the country, evaluating also the differences among regions, and in groups with different socioeconomic and behavioural characteristics.
- The collection of data based on the recall of the interviewed women can make difficult to distinguish how the test was delivered (screening programme or opportunistic) in a potentially differential way by citizenship or between different educational levels.
- The uptake obtained by the public sector, which adopts less intensive protocols and longer intervals, can be underestimated, looking at the most recent test only, because some women undergo tests at shorter intervals than recommended.

Introduction

As cervical and breast cancer screening programmes have proven effective in reducing morbidity and mortality, the European Commission recommended in 2008 that each EU Member State offer screening to its population. In accordance with these recommendations, population-based free screening programmes, with active invitation of the target population as well as quality assurance and monitoring activities, are included in the essential health care services guaranteed by the Italian National Health Service (NHS). The target population for cervical screening includes all permanent and temporary (when possible) resident women aged 25-64, and for breast screening,women aged 50-69;[1,2] the screening tests used are a Pap test every three years and mammography every two years, in accordance with EU Recommendations.[3,4] Revisions in these recommendations have been made over the last few years, resulting in the reorganization of screening programmes. As regards cervical screening, the HPV test, which allows even earlier diagnosis of pre-invasive lesions, was introduced in 2013 for women older than age 30 or 35, with a recommended interval of five years;[5,6] in 2014, therefore, only about 13% of the target population had been invited to take the HPV test. As for breast screening, the Regions of Emilia-Romagna and Piedmont extended the age of the target population to 45-74, with annual intervals for women aged 45-49.[7]

The introduction of screening programmes in Italy has been slow and characterized by profound geographical differences. The difficulties and delays in organized screening activation has favoured the spread of opportunistic screening, both by public and private providers.[8] Thus, actual screening coverage and uptake is the result of both organized and opportunistic screening models.[9] Organized public screening programmes include a monitoring system to determine exactly how many women are invited and screened in the target population, while opportunistic screening tests are registered in a way that does not allow a calculation of test coverage, and some are not registered at all.[9] Thus, the only way to have complete information about screening coverage is by interviewing the target population. Further, opportunistic screening usually adopts more intensive protocols, whose inferior efficiency has been demonstrated both in international [10,11,12] and in Italian studies [13,14,15]. As the coexistence of these two organizational models is considered unsustainable,[16] the Italian Ministry of Health has included as one of the goals of the NHS and of the regional systems the re-engineering of opportunistic screening into organised programmes.

Study objectives are: 1) to describe cervical and breast cancer screening uptake in Italy based on data from the Italian National Health Interview Survey (NHIS) conducted by National Institute of Statistics (ISTAT) in 2012-2013; 2) to study the impact of screening programme invitation coverage on uptake and individual characteristics associated with no screening.

Methods

Data sources

The study was conducted based on data of the NHIS, a population-based cross-sectional survey conducted every five years in Italy by the National Institute of Statistics.[17,18] The 2012-2013 edition collects information about screening coverage and investigates the characteristics of women who avail themselves of female cancer screening programmes, as well as other social, healthcare and behavioural covariates.

Thanks to funding from the Italian National Health Fund, the survey sample was enlarged in the 2013 survey edition, and an in-depth analysis of results from each Region was performed.

It was hypothesized that total uptake is also influenced by accessible and free screening services; thus, an ecological variable measuring the proportion of the target population invited, within the correct interval (3 years for Pap test and 2 years for mammography), by the screening programme, i.e., the invitation coverage, was created based on data from the Italian National Centre for Screening Monitoring.[8,19,20,21]

Outcomes

Cervical screening uptake is defined as the percentage of women in the target age group (aged 25-64) who received at least one Pap test in the three years prior to the interview (n=32,831, representing the population of 16,752,400 women in Italy). Breast cancer screening uptake is defined as the percentage of women in the target age group (aged 50-69) who underwent at least one mammography in the two years prior to the interview (n=16,459, representing a population of 7,925,570 women in Italy). The same age group was used to calculate the uptake in Piedmont and Emilia-Romagna, although these regions have a larger target population (women aged 45-74 years).

Three uptake indicators were identified: 1) total uptake, including services delivered in all types of healthcare facilities (public and private, upon invitation by the local health service or suggestion of private doctor or general practitioner); 2) uptake due to participation in public screening programme, including women who underwent screening "upon invitation by the public health service", as provided by one of the responses to the ISTAT questionnaire; 3) uptake in the framework of the NHS, obtained by combining women included in a public screening programme with women who performed the test in a public healthcare facility but upon the suggestion of a doctor (GP or private doctor) or on their own initiative.

Definition of individual and context factors and data analysis

A descriptive analysis evaluated the distribution of the three above-mentioned uptake indicators combined with the following fundamental dimensions: region of residence, age, citizenship, educational level, occupation, perception of economic resources, reasons hampering the pursuit of hobbies and interests, smoking habits, physical activity, weight control frequency, preventive medical examinations in the four weeks prior to the interview and general prevention tests (cholesterol, glycaemia, blood pressure) and use of complementary and alternative medicine (CAM). Hierarchical logistic models were tested by considering as first-level unit all target women, and as second level unit the Italian Regions (21 units).

Not having had a Pap test in the three years prior to the interview (two years for mammography), i.e., being under- or not screened at all, was used as outcome variable based on tests performed in screening programmes and in opportunistic setting, public and private. The above-listed categorical variables were included as first-level covariates.

Finally, in order to evaluate possible associations between the level of organised screening offered and socioeconomic access inequalities, the interaction between invitation coverage and educational level and between invitation coverage and perceived economic resources were tested. Invitation coverage was calculated as the number of invitations sent by the organised screening programme in 2011-2013 for the Pap test and in 2010-2011 for mammography divided by the total target population for each screening programme as reported by the National Institute of Statistics. The invitation coverage variable (ecological variable) was divided into two categories based on the distribution median; Pap test cut-off was 63% and mammography cut-off was 77%.

Results

Total Pap test uptake was slightly under two-thirds of the total target group (62.1%), 38.9% in the NHS and 22.2% in public screening programmes.

Total uptake ranged from 36.6% in Campania to 79.8% in Friuli-Venezia Giulia (Figure 1), while in screening programmes it ranged from 3.2% in Liguria to 53.8% in Valle d'Aosta (Figure 2). Total mammography uptake was seen in more than one-half of the target group (56.4%) and in 44.6% in the NHS, of which 29.8% was due to participation in public screening programmes. Total uptake ranged from 30.4% in Campania to 72.3% in Veneto (Figure 3), while screening programme uptake ranged from 5% in Campania to 64.3% in Trento (Figure 4).

The patterns of test uptake were very similar for Pap test and mammography in almost all regions. Total Pap test uptake increased with age up to 50 years (72.1%), and then decreased, while screening programme uptake did not decrease after age 50 (Table 1).

As regards mammography, no age differences were observed in uptake between the framework of screening programmes and of the NHS, although total coverage uptake did decrease with age.

Total Pap test and mammography uptake were higher among Italian women than foreign nationals. This difference for Pap test was larger in opportunistic screening than in screening programmes, while for mammography, a relevant gap in uptake between Italian and foreign nationals was observed also in screening programmes (30.7% vs. 20.9%).

A direct association between educational level and Pap test/mammography uptake was observed. Such an imbalance was due to lower uptake in opportunistic screening, primarily for mammography and exclusively for the Pap test.

In terms of occupation, Pap test total uptake progressively decreased from women with stronger and better paid working positions to those who lived in more unstable conditions and the unemployed. Executives, entrepreneurs, freelance professionals and office workers had higher uptake than other occupation categories, mostly due to higher uptake in private opportunistic screening. Unemployed women had low access to all screening modalities.

An association was observed between occupation and access/ uptake for mammography as well, particularly for total uptake. Perceived unsatisfactory economic resources were associated with lower total uptake, lower screening programme uptake and lower NHS uptake for both Pap test and mammography. Considering indicators related to attitude towards health and prevention, higher Pap test and mammography uptake was observed in women who had other preventive health behaviours such as preventive medical examinations in the preceding four weeks and general prevention tests, as well as more physical activity, better weight control and being a former smoker. Also, women who used CAM in the preceding three years had higher uptake.

Table 2 shows the results of the hierarchical logistic model for the probability of being under- or not screened for cervical cancer (i.e., no Pap test in the three years prior to the interview) expressed as odds ratios (OR). The intra-class correlation coefficient (ICC) calculated for the null model (without covariates) is ρ=0.06. It represents the proportion of variability that can be attributed to differences between the regions.

Low educational level, inadequate economic conditions (OR:0.80) and, especially, being a foreign national (OR:0.59) were risk factors for not having had a Pap test. Furthermore, women who declared that they had not had any general prevention tests and/ or medical examinations, did not undergo any CAM and did not do any physical activity had lower probability of undergoing the Pap test in the recommended intervals. Finally, former smokers and current smokers were more likely to access cervical cancer prevention services than non-smokers.

Women living in regions with higher invitation coverage levels than the median had a lower probability of not having the test than those women living in regions with lower invitation coverage levels (OR:0.47).

The effect of socioeconomic variables was similar in all the regions, regardless of invitation coverage levels.

As regards mammography, multivariate analysis (Table 3) confirms the results of the bivariate analysis: women aged 60-69 had a higher risk of not having had a mammography in the years preceding the interview (OR:1.34). Low educational level, inadequate economic conditions (OR:0.81) and, particularly, being a foreign national (OR:0.45) were predisposing factors for not accessing mammography. Furthermore, women who did not undergo any general prevention tests and medical examinations, did not use CAM and did not have any physical activity were less likely to have undergone mammography. Former smokers were more likely to access breast cancer prevention compared to non-smokers. Similarly, women who underwent general prevention tests or had had a medical examination in the preceding four weeks for prevention or other reasons were more likely to undergo mammography. Women living in regions with high invitation coverage had a 50% lower probability of not having had mammography when compared to women living in regions with low invitation coverage.

The effect of socioeconomic variables was similar in all the regions, regardless of invitation coverage levels. Residual variability around the intercept was observed for both for Pap test and mammography (Figure 5), with a similar geographical pattern: southern regions (except for Abruzzo, Apulia and Sardinia) show significantly higher probability of under-use of screening tests.

Discussion

Differences between geographical areas

Taking into account differences between the different Italian geographical areas, the observed national screening test uptake was 62.1% for cervical and 56.4% for breast cancer. These values are lower than the Italian and the European guidelines reference standards for screening programmes: 70% acceptable and 75% desired for breast, and 70% acceptable and 85% desired for cervical cancer.[2,4,22] Strong uptake differences still exist between regions, with a clear north-south gradient.[23] A positive trend is that differences between northern and southern Italy have diminished compared with the previous NHIS surveys due to increased coverage/access in the southern regions.[17] Differences between regions can be largely attributed to the NHS's ability to offer screening programmes that reach the target population. This hypothesis is also supported by the results of multilevel models showing how variability between regions is strongly related to

screening programme coverage in the single regions, particularly for mammography. This phenomenon can be observed at a macrolevel: those regions with higher uptake are also those with higher access in the framework of screening programmes or of the NHS. The effect on total uptake of organized screening with active invitations to the target population is well known and has been observed in all contexts.[12,24,25] Finally, it is also interesting to note that total and screening programme uptake patterns are similar in almost all regions. This suggests that where the population's attention to prevention is low, there has also been difficulty in implementing screening programmes. This result is consistent with the consolidated evidence of an association between low/changeable invitation coverage of screening programmes and low response from the population to invitations.[8,9,20,21]

It is not easy to understand the causal relationship; if a context is unfavourable to the organisation of complex and multidisciplinary paths, is this because the population in that context does not trust the NHS and thus does not respond to the invitation? Or is it because the poor organisation directly penalises compliance with programme recommendations?

Socioeconomic differences

Socioeconomic differences in uptake are still very evident, whichever variable is considered: education, citizenship, occupation or perceived economic difficulties. Even though organised screening and the NHS guarantee wider and easier access to screening, thus increasing coverage in all contexts, surprisingly, no reduction in socioeconomic differences was observed in the areas where screening programmes had higher invitation coverage. This effect on reducing access inequalities has been observed in other Italian studies.[9,26] Furthermore, the implementation of screening programmes has shown a levelling effect on breast cancer outcomes, with women in the lowest socioeconomic level attaining the same survival rates as those in the highest socioeconomic level.[27,28] A decrease in inequalities in access to effective prevention measures thanks to screening programmes and to the NHS actively promoting interventions has been observed in a number of other studies,[9,24,29,30] even though considerable exceptions or failures have also been observed.[31,32,33]

Association with other preventive health behaviours

The association with perceived economic difficulties is more difficult to interpret, as this variable combines objective available resources and factors related to more subjective perception of precarious conditions or worsening of one's economic situation. These latter factors are more related to personal coping - the capability to react to changes and difficulties - which are personal characteristics known to be associated with participation in screening; "maladaptive coping" is

associated with poor compliance with cancer screening recommendations.[34] These personal characteristics are difficult to modify through active interventions such as invitation letters or information campaigns.[34,35]

Data on the associations between uptake and single preventive health behaviours can probably be interpreted from this standpoint. In fact, such associations can be found in organised screening uptake, in public opportunistic uptake and in private opportunistic uptake as well. The existing synergy between prevention interventions and preventive health behaviours is a well-known phenomenon which offers the NHS opportunities to promote coordinated prevention initiatives.[36]

The association between both screening test uptake and being a former smoker is not surprising and has been reported by other authors;[37,38] instead, a slightly higher uptake for both Pap test and mammography in current smokers than in non-smokers is more surprising. It should be noted that the prevalence of smoking in Italy is higher among the highly educated; the difference in screening uptake thus almost disappears when adjusting for educational level. Particular attention should be paid to the association between mammography coverage and use of CAM, a partially unexpected result, as breast screening has been criticized in the last few years by groups concerned with overdiagnosis and overtreatment and against the medicalisation of the healthy population.[39,40] These opinions, which are not against technology per se, are welcome in cultural contexts that refuse a technological approach to life and health care and that are often attracted by CAM.[41] A positive association between CAM and mammography coverage thus suggests that a lack of coverage is, to a large degree, not a conscious choice but instead due to the lack of access to the service.

Limitations and strengths of the study and comparison with other data

The main limitations of the data used in the present study are related to data collection techniques, namely a retrospective study based on the recall of the interviewed women. When recalling past events, it can be difficult to distinguish between different organizational and administrative ways of how the test was delivered. For example, a test undergone in the framework of a screening programme could be confused with a test provided by the NHS outside an organised programme (in some local health services, the patient cannot perceive this difference). This observation does not influence total uptake but can generate incorrect classification of access modalities that can differ between Italian women and foreign nationals or between different educational levels. In fact, it can be difficult to define just what a "screening programme" is, resulting in a possible misunderstanding and thus confusing it with a more general access to a public health centre, particularly by less educated women or foreigner nationals with linguistic barriers. For this reason, most of the analysis was conducted by using the two indicators "public sector uptake" and "screening programme

uptake" to give an idea of the range of the actual data. Furthermore, some women undergo tests at shorter intervals than recommended,[9,13] which can mask part of the uptake obtained by the NHS when we look at the most recent test only, as in this survey. In fact, if a woman has already undergone a test performed in the NHS and then undergoes an opportunistic test before the recommended interval has expired, she will register as covered by the opportunistic test and not by the previous NHS test. Thus, we underestimate the coverage by the public sector, which adopts less intensive protocols and longer intervals.[13,26,42] Furthermore, a survey with less stringent questions to identify the date of the last screening test may overestimate coverage due to telescoping effect (women reporting having undergone the test more recently than in fact they have), as noted in a previous Italian survey.[42] Indeed, the questions about the last screening test are posed slightly differently in the Italian NHIS and in the routine surveillance system – the PASSI survey – managed by the local health authorities.[26] This surveillance reports an overall uptake of 77% and 70% for cervical and breast cancer screening, respectively. It is also important to underline that the HPV test, which was authorized as a primary screening test instead of the Pap test in women older than 30-35 years in January 2013 by the Italian Ministry of Health, was available only through some pilot projects until 2014. Given that the NHIS interviews were conducted in 2012/13 and that the questions referred to tests undergone in the three preceding years, obviously very few women had been invited to HPV screening at that point.[20,26,42] Among the strengths of this study to be mentioned is the enormous information potential of the ISTAT survey, both at the individual and at the family level, offering a very rich description of individual women, their families and their socioeconomic status. This is the first scientific paper analysing the association between screening uptake and different sections of the NHIS questionnaire.

Another strong point is the inclusion of an ecological variable on the screening offered, from a second data source. The joint use of these two data sources made it possible to estimate the impact of screening programmes on overall screening uptake and on differences in screening uptake between regions, groups with different socioeconomic and behavioural characteristics.

Conclusions

Total coverage observed through the Italian NHIS is below the desired and acceptable levels recommended by the European Commission.

Screening programmes increase uptake and have the potential, when correctly implemented, to decrease geographical inequalities, although not those differences caused by individual attitudes towards health and prevention.

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Contributors

AP, PGR and LG designed and initiated the study and wrote the manuscript. LF extracted the data, conducted statistical analysis, interpreted the findings and reviewed/edited the manuscript. BG conducted statistical analysis. ADN reviewed and edited the manuscript. MZ and CM contributed to the discussion and critically reviewed the final manuscript. All authors read and approved the final manuscript.

Data sharing statement

The analyses were performed using data based on ISTAT's surveys. In particular, we used ISTAT's standard files (issued upon request with a valid reason for research purposes and released free of charge and in compliance with the principle of statistical secrecy and protection of personal data). To acquire such files it is necessary to register at the area of the ISTAT website dedicated to them and to accept the terms of use. Data are available in different formats (TXT, STATA, SAS, R).

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References

1. Osservatorio Nazionale Screening. 2014. I programmi di screening in Italia. http://www.osservatorionazionalescreening.it/sites/default/files/allegati/Screening_2014_web.pdf
2. Giorgi D, Giordano L, Ventura L, et al. Mammography breast cancer screening in Italy: 2010 survey. *Epidemiol Prev* 2012;361:8–27.
3. von Karsa L, Anttila A, Ronco G, et al., eds. Cancer screening in the European Union. Report on the implementation of the Council Recommendation on cancer screening. First report. Luxembourg: European Commission, 2008.
4. Perry N, Broeders M, de Wolf C, et al., eds. European guidelines for quality assurance in breast cancer screening and diagnosis. Luxembourg: European Commission. Office for Official Publications of the European Communities, 2006.
5. Ronco G, Biggeri A, Confortini M, et al. [Health technology assessment report: HPV DNA based primary screening for cervical cancer precursors]. *Epidemiol Prev* 2012;36:e1–e72.
6. von Karsa L, Arbyn A, De Vuyst H, et al. Executive summary. In: Anttila A, Arbyn M, De Vuyst H, et al., eds. European guidelines for quality assurance in cervical cancer screening. Luxembourg: Publications Office of the European Union, 2015, Second edition – supplements: pp. XIII–XXIV.
7. Distante V, Ciatto S, Frigerio A, et al. [Recommendations of a national Italian consensus conference on the opportunity of extending screening service by mammography to 40-49 and 70-74 years of age women]. *Epidemiol Prev* 2007;31:15–22.
8. Zappa M, Carozzi FM, Giordano L, et al. The diffusion of screening programmes in Italy, years 2011-2012. *Epidemiol Prev* 2015;39:5–8.
9. Giorgi Rossi P, Camilloni L, Cogo C, et al. [Methods to increase participation in cancer screening programmes]. *Epidemiol Prev* 2012;36:1–104.
10. Smith-Bindman R, Chu PW, Miglioretti D, et al. Comparison of Screening Mammography in the United States and the United Kingdom. *JAMA* 2003;290:2129–37.
11. Hofvind S, Vacek PM, Skelly J, et al. Comparing screening mammography for early breast cancer detection in Vermont and Norway. *J Natl Cancer Inst* 2008;100:1082–91. doi: 10.1093/jnci/djn224.
12. Nygård JF, Skare GB, Thoresen SØ. The cervical cancer screening programme in Norway, 1992-2000: changes in Pap smear coverage and incidence of cervical cancer. *Med Screen* 2002;9(2):86-91.
13. Ronco G, Segnan N, Giordano L, et al. Interaction of spontaneous and organised screening for

cervical cancer in Turin, Italy. *Eur J Cancer* 1997;33:1262–7.

14. Giorgi Rossi P, Chini F, Barca A, et al. [Efficacy of disease management profiles. The mammographic screening program of Lazio]. *Tumori* 2008;94(3):297-303.
15. Giorgi Rossi P, Federici A, Farchi S, et al. The effect of screening programmes on the treatment of benign breast neoplasms: observations from current practice in Italy. *J Med Screen* 2006;13(3):123-8.
16. Martin-Moreno JM, Anttila A, von Karsa L, et al. Cancer screening and health system resilience: keys to protecting and bolstering preventive services during a financial crisis. *Eur J Cancer* 2012;48(14):2212-8. doi: 10.1016/j.ejca.2012.02.060.
17. ISTAT. 2006. Fattori di rischio e tutela della salute — Indagine multiscopo sulle famiglie italiane "Prevenzione dei tumori femminili: ricorso a pap test e mammografia" anni 2004/2005. http://www3.istat.it/salastampa/comunicati/non_calendario/20061204_00/testointegrale.pdf
18. ISTAT. 2013. Multiscopo sulle famiglie: condizioni di salute e ricorso ai servizi sanitari. http://siqual.istat.it/SIQual/visualizza.do?id=0071201
19. Ronco G, Giorgi Rossi P, Giubilato P, et al. A first survey of HPV-based screening in routine cervical cancer screening in Italy. *Epidemiol Prev* 2015;39:77–83.
20. Ronco G, Giubilato P, Carozzi F, et al. Extension of organized cervical cancer screening programmes in Italy and their process indicators, 2011-2012 activity. *Epidemiol Prev* 2015;39:61–76.
21. Ventura L, Giorgi D, Giordano L, et al. Mammographic breast cancer screening in Italy: 2011-2012 survey. *Epidemiol Prev* 2015;39:21–9.
22. Anttila A, Ronco G, Nicula F, et al. Organization of cytology-based and HPV-based cervical cancer screening. In: Anttila A, Arbyn M, De Vuyst H, et al., eds. European guidelines for quality assurance in cervical cancer screening. Luxembourg: Publications Office of the European Union, 2015, Second edition – supplements: pp. 69–108.
23. Giorgi Rossi P, Carrozzi G, Federici A, et al. Invitation coverage and participation in Italian cervical, breast and colorectal cancer screening programmes. *J Med Screen* 2017;Jan1. doi: 10.1177/0969141317704476.
24. Palència L, Espelt A, Rodríguez-Sanz M, et al. Socio-economic inequalities in breast and cervical cancer screening practices in Europe: influence of the type of screening program. *Int J Epidemiol* 2010;39:757–65. doi: 10.1093/ije/dyq003.
25. Ferroni E, Camilloni L, Jimenez B, et al. How to increase uptake in oncologic screening: a systematic review of studies comparing population-based screening programs and spontaneous access. *Prev Med* 2012;55:587–96. doi: 10.1016/j.ypmed.2012.10.007.

26. Carrozzi G, Sampaolo L, Bolognesi L, et al. Cancer screening uptake: association with individual characteristics, geographic distribution, and time trends in Italy. *Epidemiol Prev* 2015;39:9–18.
27. Pacelli B, Carretta E, Spadea T, et al. Does breast cancer screening level health inequalities out? A population-based study in an Italian region. *Eur J Public Health* 2014;24:280–5. doi: 10.1093/eurpub/ckt119.
28. Puliti D, Miccinesi G, Manneschi G, et al. Does an organised screening programme reduce the inequalities in breast cancer survival? *Ann Oncol* 2012;23:319–23. doi: 10.1093/annonc/mdr121.
29. Spadea T, Bellini S, Kunst A, et al. The impact of interventions to improve attendance in female cancer screening among lower socioeconomic groups: a review. *Prev Med* 2010;50:159–64. doi: 10.1016/j.ypmed.2010.01.007.
30. Giorgi Rossi P, Baldacchini F, Ronco G. The Possible Effects on Socio-Economic Inequalities of Introducing HPV Testing as Primary Test in Cervical Cancer Screening Programs. *Front Oncol* 2014;4:20. doi: 10.3389/fonc.2014.00020.
31. Lagerlund M, Bellocco R, Karlsson P, et al. Socio-economic factors and breast cancer survival - a population-based cohort study (Sweden). *Cancer Causes Control* 2005;16:419–30.
32. Louwman WJ, van de Poll-Franse LV, Fracheboud J, et al. Impact of a programme of mass mammography screening for breast cancer on socio-economic variation in survival: a population-based study. *Breast Cancer Res Treat* 2007;105:369–75.
33. Halmin M, Bellocco R, Lagerlund M, et al. Long-term inequalities in breast cancer survival--a ten year follow-up study of patients managed within a National Health Care System (Sweden). Acta Oncol 2008;47:216–224. doi: 10.1080/02841860701769768.
34. Federici A, Guarino A, Serantoni G. Adesione ai programmi di screening di prevenzione oncologica: proposta di una modellizzazione dei risultati di revisione della letteratura secondo il Modello PRECEDE-PROCEED. *Epidemiol Prev* 2012;36:1–104.
35. Federici A, Poletti P, Guarino A, et al. Garantire la partecipazione consapevole. In: Federici A, ed. Screening - Profilo complesso di assistenza. Roma: Il Pensiero Scientifico, 2007: pp. 252–257.
36. Bankhead CR, Brett J, Bukach C, et al. The impact of screening on future health-promoting behaviours and health beliefs: a systematic review. *Health Technol Assess* 2003;7:1–92.
37. Venkataraman K, Wee HL, Ng SHX, *et al.* Determinants of individuals' participation in integrated chronic disease screening in Singapore. *J Epidemiol Community Health* 2016;70:1242–50. doi:10.1136/jech-2016-207404

38. Labeit A, Peinemann F, Baker R. Utilisation of preventative health check-ups in the UK: findings from individual-level repeated cross-sectional data from 1992 to 2008. *BMJ Open* 2013;3:e003387. doi:10.1136/bmjopen-2013-003387
39. Grady D. Look for cancer, and find it! In: New York Times, 2014. http://well.blogs.nytimes.com/2014/04/07/look-for-cancer-and-find-it/
40. Gøtzsche PC, Hartling OJ, Nielsen M, Brodersen J, Jørgensen KJ. Breast screening: the facts--or maybe not. BMJ 2009;338:b86–b86. doi: 10.1136/bmj.b86.
41. Volpi R. L'amara medicina. Come la sanità italiana ha sbagliato strada. Milano: Feltrinelli, 2008.
42. Giorgi Rossi P, Esposito G, Brezzi S, et al. Estimation of Pap-test coverage in an area with an organised screening program: challenges for survey methods. *BMC Health Serv Res* 2006;6:36.

Table 1. Pap test and mammography: total uptake, uptake in the National Health Service and public screening coverage, by educational level, occupation, and perception of economic family resources. Italy, 2012-2013.

	PAP TEST			MAMMOGRAPHY		
		uptake in the NHS			uptake in the NHS	
	Total uptake	Of which public screening coverage	Total	Total uptake	Of which public screening coverage	Total
Age						
25-29	48.5	13.3	28.2			
30-34	58.1	18.6	35.7			
35-39	63.8	19.9	37.3			
40-44	65.1	21.9	38.2			
45-49	72.1	23.6	42.8			
50-54	69.1	26.6	45.2	60.5	28.1	44.9
55-59	60.2	25.9	41.4	57.7	29.8	44.4
60-64	53.3	25.7	39.1	55.4	32.2	44.8
65-69				50.7	29.4	41.6
Citizenship						
Italian	63.2	26,0	37.4*	55.9	30.7	44.2
Foreign national	52.2	23.8	40.6	41.4	20.9	32.4
Educational level						
Degree	68.6	20.2	37.2	65.5	29.9*	46.5
School-leaving certificate	64.6	21.5	37.4	60.8	28.8	44.3
Compulsory education	57.8	23.6	40.8	53.3	30.2	43.5
Occupation						
Executive, Entrepreneur, Freelance professional	74.4	20.1	35.4	65.1	27.8	40.9
Office worker	73,0	23.9	40.4	68.1	33.1	49.7
Workman, Apprentice, Other	64.1	28.2	45.8	58.2	34.6	48.6
Independent businessman, Homecare assistant, Cooperative member	67.5	24.7	40.2	60.5	35.7	50.4
Contract worker	60.2	20.3	34.4	59.9	21.3	40.4
Not employed	54.1	19.5	36.3	52.8	28.3	41.9
Perceived economic resources						
Excellent/Adequate	66.0	25.6	41.8	60.9	32.4	46.9
Scarce/Insufficient	53.9	21.9	38.8	48.6	25.4	39.2
Reasons hampering pursuit of hobbies or interests						
Other	60.3	22.0	38.7	55.4	29.5	43.3
Too busy	67.6	22.9	39.5	61.1	31.3	47.7
Smoking habits						
Smoker	62.2	21.9	38.6	56.6	30.9	45,0
Former smoker	70.9	26.8	43.8	63.8	35.2	51.3
Non-smoker	59.6	21.1	37.6	53.8	27.7	41.3
Physical activity						
No	55.9	19.4	36.2	47.7	24,0	37.3
Yes	67.9	24.8	41.4	64.9	35.5	50.6

Weight control						
Rarely or never	56.9	20.7	36.1	48.7	25.2	37.7
Weight controlled	65.2	23.1	40.6	61.4	32.9	48.2
Preventive medical examinations in the preceding 4 weeks						
No examination	58.0	20.9	37,0	52.2	28.2	41,0
At least one examination	75.0	23.7	41.8	65.8	32.9	49.5
Other examinations	68.7	25.5	43.4	61.8	32.1	48.5
General prevention medical tests						
No test	43.7	16,0	28.5	35,0	18.9	27.2
1 or 2 tests	56.9	22.2	37.5	50.2	31.3	42.5
All tests	64.7	23,0	40.3	57.5	30.2	44.8
Use of complementary and alternative medicine						
Never used or more than three years ago	60.0	21.3	38.2	54.9	29.1	43,0
At least once in the last three years	79.2	29.6	44.8	68.5	35.9	52.2
Total	**62.1**	**22.2**	**38.9**	**56.4**	**29.8**	**44,0**

All differences are statistically significant, except *

Table 2. Multilevel logistic random intercept model for Pap test. Model on not having had the test in the three years prior to interview. Italy, 2012-2013.

Variable		Adjusted OR	95% CI	
Individual				
Age group	25-34	1		
	35-44	0.69	0.64	0.75
	45-54	0.53	0.49	0.57
	55-64	1.01	0.93	1.09
Citizenship	Foreign national	1		
	Italian	0.59	0.54	0.65
Educational level	Compulsory education	1		
	School-leaving certificate	0.89	0.84	0.95
	Degree	0.86	0.79	0.93
Perceived economic resources	Scarce, Absolutely insufficient	1		
	Excellent, adequate	0.80	0.76	0.85
Occupation	Unemployed	1		
	Executive, Entrepreneur, Freelance professional	0.93	0.76	1.15
	Office worker	0.74	0.65	0.86
	Workman, Apprentice, Other	0.85	0.76	0.95
	Independent businessman, Homecare assistant, Cooperative member	0.87	0.81	0.94
	Contract worker	0.78	0.73	0.84
Reasons hampering pursuit of hobbies or interests	Other reasons	1		
	Too busy	0.84	0.79	0.89
Smoking habits	Non-smoker	1		
	Former smoker	0.73	0.69	0.78
	Smoker	0.93	0.87	0.99
Physical activity	No	1		
	Yes	0.86	0.82	0.91
Weight control	Rarely or never	1		
	Periodically	0.80	0.76	0.84
Preventive medical examinations in the preceding 4 weeks	No examination	1		
	Other reasons	0.70	0.66	0.75
	Preventive examination	0.57	0.52	0.63
General prevention medical tests	No test	1		
	1 or 2 tests	0.71	0.62	0.80
	All tests	0.54	0.50	0.58
Use of complementary and alternative medicine	Never used or more than three years ago	1		
	At least once in the last three years	0.71	0.65	0.77
Contextual				
Invitation coverage in the period 2011-13	Within the median	1		
	above the median	0.472	0.32	0.697
Random effect				
		Estimate	**Standard error**	**P-value**
$\alpha_{i,\ regions}$		0.209	0.066	<0.01

ICC - Intraclass Correlation Coefficient (ρ)	0.0597

Table 3. Multilevel logistic random intercept model for mammography. Model on lack of coverage in the two years before interview. Italy, 2012-2013.

Variable		Adjusted OR	95% CI	
Individual				
Age group	50-59	1		
	60-69	1.34	1.24	1.44
Citizenship	Foreign national	1		
	Italian	0.45	0.37	0.54
Educational level	Compulsory education	1		
	School-leaving certificate	0.92	0.85	1.01
	Degree	0.77	0.68	0.88
Perceived economic resources	Scarce, Absolutely insufficient	1		
	Excellent, adequate	0.81	0.75	0.87
Occupation	Unemployed	1		
	Executive, Entrepreneur, Freelance professional	0.68	0.44	1.06
	Office worker	1.01	0.80	1.27
	Workman, Apprentice, Other	0.98	0.83	1.16
	Independent businessman, Homecare assistant, Cooperative member	0.91	0.80	1.03
	Contract worker	0.81	0.73	0.91
Reasons hampering pursuit of hobbies or interests	Other reasons	1		
	Too busy	0.87	0.80	0.96
Smoking habits	Non-smoker	1		
	Former smoker	0.85	0.78	0.92
	Smoker	1.00	0.91	1.09
Physical activity	No	1		
	Yes	0.73	0.68	0.78
Weight control	Rarely or never	1		
	Periodically	0.75	0.70	0.80
Preventive medical examinations in the last 4 weeks	No examination	1		
	Other reasons	0.66	0.61	0.71
	Preventive examination	0.64	0.57	0.71
General prevention medical tests	No test	1		
	1 or 2 tests	0.70	0.55	0.89
	All tests	0.50	0.42	0.59
Use of complementary and alternative medicine	Never used or more than three years ago	1		
	At least once in the last three years	0.82	0.73	0.92
Contextual				
Invitation coverage in the period 2011-13	Within the median	1		
	Above the median	0.50	0.36	0.70
Random effect				
		Estimate	**Standard error**	**P-value**
$\alpha_{i,\ regions}$		0.136	0.045	<0.01
ICC- Intraclass Correlation Coefficient (ρ)		0.040		

Figure legends

Figure 1. Utilization of Pap test (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

Figure 2. Utilization of Pap test (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

Figure 3. Utilization of mammography (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

Figure 4. Utilization of mammography (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

Figure 5. Level 2 residuals of hierarchical models for Pap test and mammography. Italy, 2012-2013.

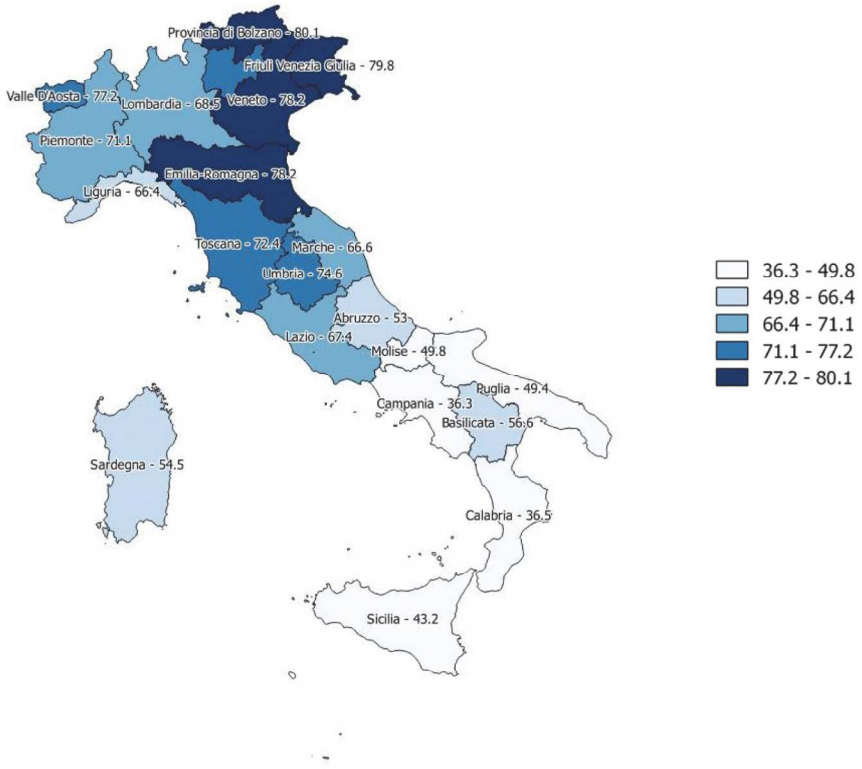

Figure 1. Utilization of Pap test (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

160x126mm (300 x 300 DPI)

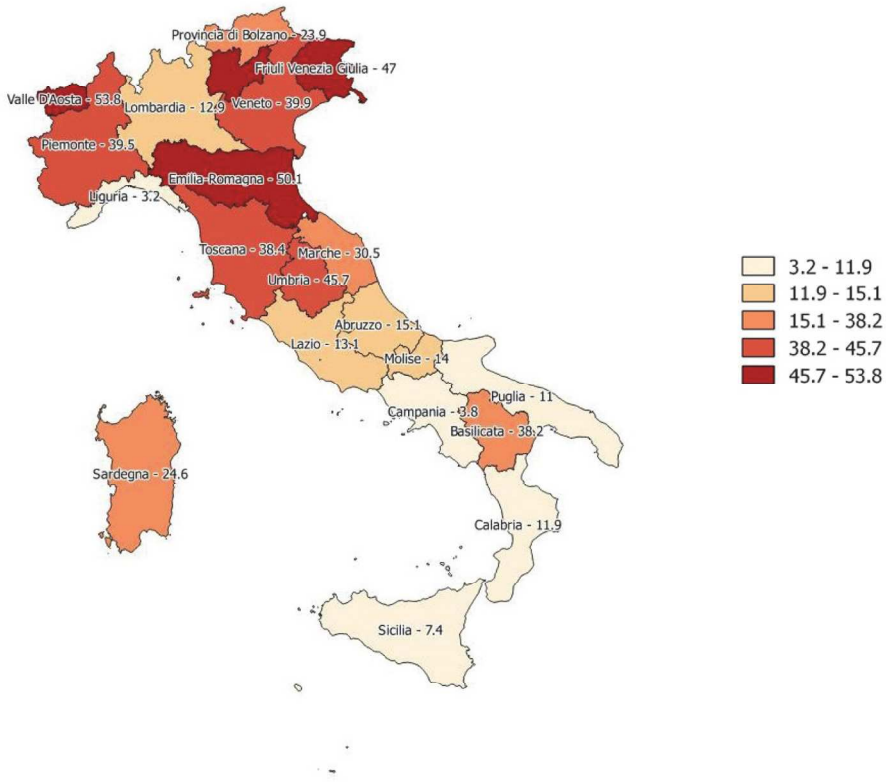

Figure 2. Utilization of Pap test (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

157x125mm (300 x 300 DPI)

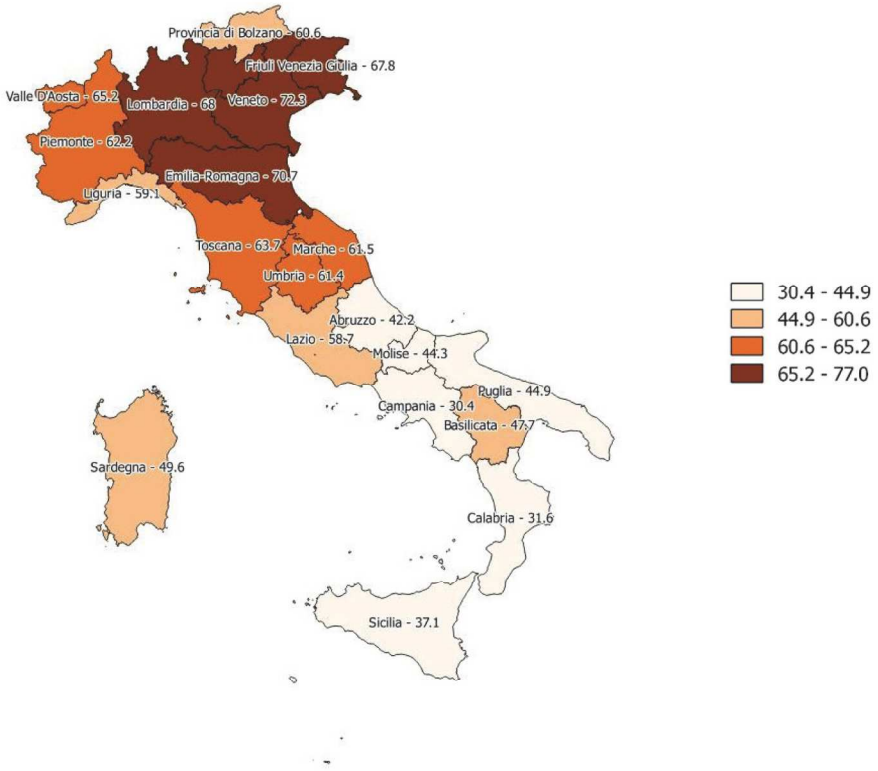

Figure 3. Utilization of mammography (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

159x124mm (300 x 300 DPI)

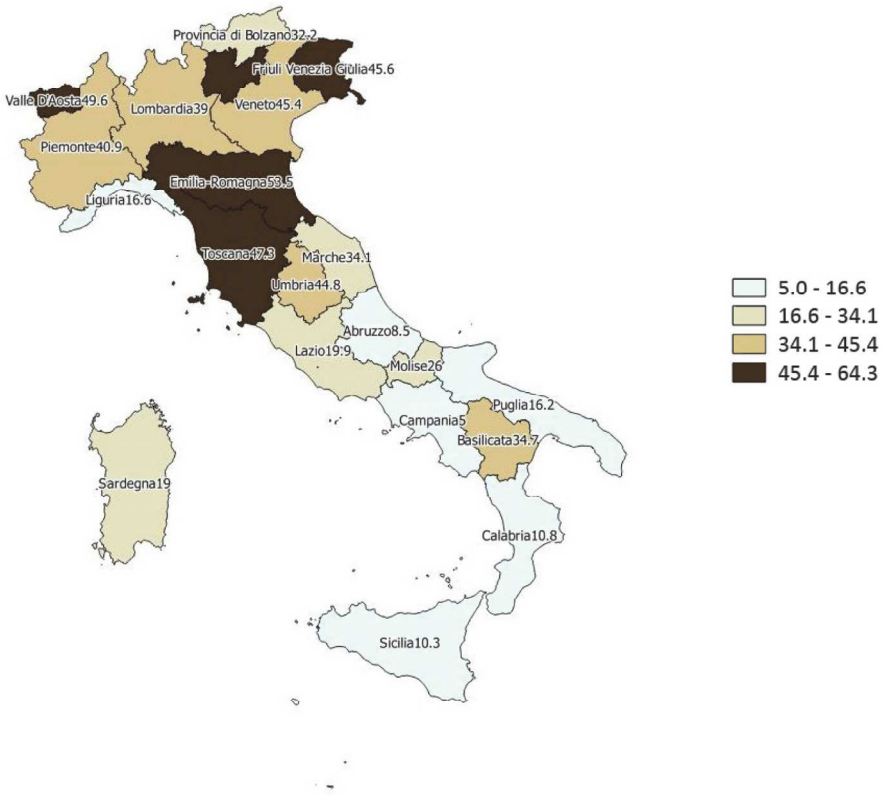

Figure 4. Utilization of mammography (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

154x125mm (300 x 300 DPI)

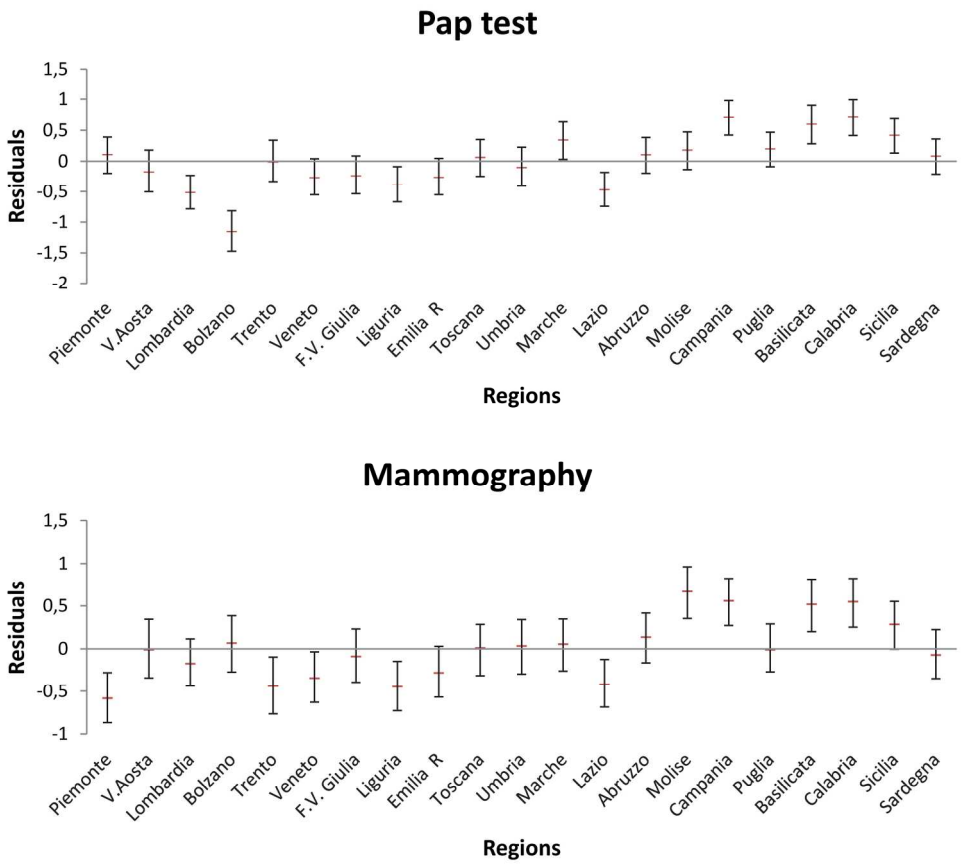

Figure 5. Level 2 residuals of hierarchical models for Pap test and mammography. Italy, 2012-2013.

175x158mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods	

taking account of sampling strategy

(*e*) Describe any sensitivity analyses

Continued on next page

Results			**Page number**
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	6-7
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-8
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Geographic and socioeconomic differences in uptake of Pap test and mammography in Italy: results from the National Health Interview Survey

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology, Health services research, Oncology
Keywords:	Pap test, mammography, socioeconomic, immigrants, geographic, Italy

Title

Geographic and socioeconomic differences in uptake of Pap test and mammography in Italy: results from the National Health Interview Survey

Short title

Factors associated with Pap test and mammography uptake

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Word count: 3,752

Number of tables: 4

Number of figures: 5

Abstract

Objective: The Italian National Health Service (NHS) instituted cervical and breast cancer screening programmes in 1999; the local health authorities have a mandate to implement these screening programmes by inviting all women aged 25-64 for a Pap test every three years (or for an HPV test every five years) and women aged 50-69 for a mammography every two years. However, the implementation of screening programmes throughout the country is still incomplete. The study aims to: 1) describe cervical and breast cancer screening uptake; 2) evaluate geographic and individual socioeconomic difference in screening uptake.

Methods: Data both from the Italian National Health Interview Survey (NHIS) conducted by the National Institute of Statistics (Istat) in 2012-2013 and from the Italian National Centre for Screening Monitoring (INCSM) were used. The NHIS interviewed a national representative random sample of 32,831 women aged 25-64 and of 16,459 women aged 50-69. Logistic multilevel models were used to estimate the effect of socioeconomic variables and behavioural factors (level 1) on screening uptake. Data on screening invitation coverage at the regional level, taken from INCSM, were used as ecological (level 2) covariates.

Results: Total three-year Pap test and two-year mammography uptake was 62.1% and 56.4%, respectively; screening programmes accounted for 1/3 and 1/2 of total test uptake, respectively. Strong geographical differences were observed. Uptake was associated with high educational levels, healthy behaviours, being a former smoker, and being Italian vs. foreign national. Differences in uptake between Italian regions were mostly explained by the invitation coverage to screening programmes.

Conclusions: The uptake of both screening programmes in Italy is still under acceptable levels. Screening programme implementation has the potential to reduce the health inequalities gap between regions but only if uptake increases.

Keywords: Pap test, mammography, socioeconomic, immigrants, geographic, Italy

Strengths and limitations of this study

- The large amount of information derived from NHIS survey allowed us to investigate inequities in screening uptake in Italy thoroughly for the first time.
- The joint use of two data sources enabled estimating the impact of screening programmes on uptake in the country, evaluating also the differences between regions, and in groups with different socioeconomic and behavioural characteristics.
- The collection of data based on the recall of the interviewed women can make it difficult to distinguish how the test was delivered (screening programme or opportunistic) in a potentially differential way by citizenship or between different educational levels.
- The uptake obtained by the public sector, which adopts less intensive protocols and longer intervals, may be underestimated, looking at the most recent test only, because some women undergo tests at shorter intervals than recommended.

Introduction

As cervical and breast cancer screening programmes have proven effective in reducing morbidity and mortality, the European Commission recommended in 2003 that each EU Member State offer screening to its population. In accordance with these recommendations, population-based free screening programmes, with active invitation of the target population as well as quality assurance and monitoring activities, are included in the essential health care services guaranteed by the Italian National Health Service (NHS). The target population for cervical screening includes all permanent and temporary (when possible) resident women aged 25-64, and for breast screening, women aged 50-69;[1,2] the screening tests used are a Pap test every three years and mammography every two years, in accordance with EU Recommendations (see box 1).[3,4]

The introduction of screening programmes in Italy has been slow and characterized by profound geographical differences. The difficulties and delays in organized screening activation have favoured the spread of opportunistic screening, both by public and private providers.[5] Thus, actual screening coverage and uptake is the result of both organized and opportunistic screening models.[6] Organized public screening programmes include a monitoring system to determine exactly how many women are invited and screened in the target population, while opportunistic screening tests are registered in a way that does not allow a calculation of test coverage, and some are not registered at all.[6] Thus, the only way to have complete information about screening coverage is by interviewing the target population. The spread of opportunistic testing and the progressive implementation of organized screening has led to a marked increase in test coverage. In 1994, the once-in-a-lifetime Pap test (ages 25-64) uptake was 60% and mammography (ages 50-69) uptake was 44%, virtually all due to opportunistic screening. In 2004, both tests had an uptake of 71%, with organised screening playing a major role, particularly for mammography. [7] Nevertheless, the role of the two models in maintaining high test uptake now in Italy is unclear, and a previous project, [8] based on the Green and Kreuter model[9] demonstrated a negative association between organized and opportunistic screening.

Furthermore, the association between socioeconomic factors and screening participation differs between opportunistic screening and organized programmes. In fact, organized programmes have shown to reduce inequality in access, particularly for mammography.[10] Furthermore, studies on the association between healthy behaviours and screening uptake have shown inconsistent results;[11] the heterogeneity could be due to the different screening settings, with organized programmes showing no or small differences,[12] particularly in colorectal cancer screening.[13,14] In Italy, the coexistence of opportunistic and organized screening and the wide variation among regions in the level of

organised screening implementation makes it possible to study how these two ways of delivering screening interact with the known determinants of screening uptake.

Study objectives are: 1) to describe cervical and breast cancer screening uptake in Italy based on data from the Italian National Health Interview Survey (NHIS) conducted by National Institute of Statistics (Istat) in 2012-2013. We distinguish overall uptake and uptake within organised screening programmes; 2) study geographic and individual socioeconomic difference in screening uptake, and the impact of screening programme invitation coverage on these determinants.

Methods

Data sources

This study is part of epidemiological and political analyses of the barriers to implementation of and participation in screening programmes in Italy conducted within the framework of the Green and Kreuter model.[9,15]

The study was conducted based on data from the NHIS, a population-based cross-sectional survey conducted every five years in Italy by the Istat[16,17] and from the Italian National Centre for Screening Monitoring (INCSM). The 2012-2013 edition of the NHIS collected information about screening coverage and investigated the characteristics of women who availed themselves of female cancer screening programmes, as well as other social, healthcare and behavioural covariates.

Thanks to funding from the Italian National Health Fund, the survey sample was enlarged in the 2013 survey edition, and an in-depth analysis of results from each Region was performed.

It was hypothesized that total uptake is also influenced by accessible, free screening services. Thus, a variable measuring the proportion of the target population invited by the screening programme within the correct interval (the invitation coverage) at the regional level (ecological variable) was created based on data from the INCSM.[11,18,19,20] The intervals considered were 3 years for Pap test and 2 years for mammography.

Patient and Public Involvement

No patients neither healthy individuals were involved for this study.

Outcomes

Cervical screening uptake is defined as the percentage of women in the target age group (aged 25-64) who received at least one Pap test in the three years prior to the interview (n=32,831, representing the population of 16,752,400 women in Italy). Breast cancer screening uptake is defined as the percentage of women in the target age group (aged 50-69) who underwent at least

one mammography in the two years prior to the interview (n=16,459, representing a population of 7,925,570 women in Italy).

Three uptake indicators were identified, based on the responses to the NHIS questionnaire: 1) total uptake, including services delivered in all types of healthcare facilities (public or private) and performed upon invitation of public screening programme, on suggestion of general practitioner or private doctor or on own initiative); 2) uptake in a public healthcare facility, upon the suggestion of a general practitioner or private doctor or on own initiative; 3) uptake in a public healthcare facility, upon invitation to public screening programme.

Definition of individual and context factors and data analysis

A descriptive analysis evaluated the distribution of the three above-mentioned uptake indicators combined with the following fundamental dimensions: region of residence, age, citizenship, educational level, occupation, perception of economic resources, reasons hampering the pursuit of hobbies and interests (considered a proxy of availability of time), smoking habits, physical activity, weight control frequency, preventive medical examinations in the four weeks prior to the interview, general prevention tests (cholesterol, glycaemia, blood pressure) in the four weeks prior to the interview and use of complementary and alternative medicine (CAM). Regarding preventive medical examinations, we classified the variable in three categories, based on the answers to the questionnaire: 1) no examination, 2) at least one preventive examination (in the absence of disorders or symptoms), 3) examinations for other reasons (diseases or disorders, prescriptions, medical certificates, other). Hierarchical logistic models, adjusted for all the above-mentioned covariates, were tested to evaluate geographic and socioeconomic differences in Pap test and mammography uptake. The first-level unit was all target women and the second level unit was the Italian Regions (21 units). Hierarchical models were used because it can be hypothesized that Pap test and mammography uptakes have a structure of correlation between individuals that differs between regions of residence both for the effect of the heterogeneity of the public screening programme organization and for the homogeneity in the population's socioeconomic and demographic characteristics within each region. We estimated the geographical differences as regional residual around level 1 intercept, which can be interpreted as the national mean effect after adjustment for all the covariates considered. We also calculated the intra-class correlation coefficient (ICC) for the null model (without covariates), which represents the proportion of variability that can be attributed to differences between the regions. The effect of socioeconomic level was evaluated by the estimation of the odds ratios (OR) related to citizenship, educational level, perception of economic resources and occupation.

Having had a Pap test in the three years prior to the interview (two years for mammography) was used as outcome variable based on tests performed in screening programmes and in opportunistic settings, both public and private. The above-listed categorical variables were included as first-level covariates.

Finally, in order to evaluate possible associations between the level of organised screening offered and socioeconomic access inequalities, the interaction between invitation coverage and educational level and between invitation coverage and perceived economic resources were tested. Invitation coverage was calculated as the number of invitations sent by the organised screening programme in 2011-2013 for the Pap test and in 2010-2011 for mammography divided by the total target population for each screening programme as reported by the Istat. The regional invitation coverage variable was divided into two categories based on the distribution median; Pap test cut-off was 63% and mammography cut-off was 77%.

Results

Total Pap test uptake was slightly under two-thirds of the total target group (61.1%), 38.9% in the NHS and 22.2% in public screening programmes.

Total uptake ranged from 36.6% in Campania to 79.8% in Friuli-Venezia Giulia (Figure 1), while in screening programmes it ranged from 3.2% in Liguria to 53.8% in Valle d'Aosta (Figure 2). Total mammography uptake was seen in more than one-half of the target group (56.4%) and in 44.6% in the NHS, of which 29.8% was due to participation in public screening programmes. Total uptake ranged from 30.4% in Campania to 72.3% in Veneto (Figure 3), while screening programme uptake ranged from 5% in Campania to 64.3% in Trento (Figure 4).

The patterns of test uptake were very similar for Pap test and mammography in almost all regions. Total Pap test uptake increased with age up to 50 years (72.1%), and then decreased, while screening programme uptake did not decrease after age 50 (Table 1).

As regards mammography, no age differences were observed in uptake between the frameworks of screening programmes and of the NHS, although total coverage uptake did decrease with age.

Total Pap test and mammography uptake were higher among Italian women than foreign nationals. This difference for Pap test was larger in opportunistic screening than in screening programmes, while for mammography, a relevant gap in uptake between Italian and foreign nationals was observed also in screening programmes (30.7% vs. 20.9%).

A direct association between educational level and Pap test/mammography uptake was observed. Such an imbalance was due to lower uptake in opportunistic screening, primarily for mammography and exclusively for the Pap test.

In terms of occupation, Pap test total uptake progressively decreased from women with stronger and better paid working positions to those who lived in more unstable conditions and the unemployed. Executives, entrepreneurs, freelance professionals and office workers had higher uptake than other occupation categories, mostly due to higher uptake in private opportunistic screening. Unemployed women had low access to all screening modalities.

An association was observed between occupation and access/ uptake for mammography as well, particularly for total uptake. Perceived unsatisfactory economic resources were associated with lower total uptake, lower screening programme uptake and lower NHS uptake for both Pap test and mammography. Considering indicators related to attitude towards health and prevention, higher Pap test and mammography uptake was observed in women who had other preventive health behaviours such as preventive medical examinations in the preceding four weeks and general prevention tests, as well as more physical activity, better weight control and being a former smoker. Also, women who used CAM in the preceding three years had higher uptake.

Table 2 shows the results of the hierarchical logistic model for the probability of being screened for cervical cancer (i.e., Pap test in the three years prior to the interview) expressed as OR.

High educational level, adequate economic conditions (OR:1.25) and especially being Italian (OR:1.69) were factors associated with higher probability for having had a Pap test. Furthermore, women who declared that they had had any general prevention tests and/ or medical examinations, used any CAM and did any physical activity had higher probability of undergoing the Pap test in the recommended intervals. Finally, former smokers and current smokers were more likely to access cervical cancer prevention services than non-smokers.

Women living in regions with higher invitation coverage levels than the median had a higher probability of having the test than those women living in regions with lower invitation coverage levels (OR:2.12).

The effect of socioeconomic variables was similar in all the regions, regardless of invitation coverage levels.

As regards mammography, multivariate analysis (Table 3) confirms the results of the bivariate analysis: women aged 60-69 had a lower probability of having had a mammography in the years preceding the interview (OR:0.75). High educational level, adequate economic conditions (OR:1.23) and particularly being Italian (OR:2.22) were predisposing factors for accessing mammography. Furthermore, women who did any physical activity were more likely to have undergone mammography (OR:1.37). Former smokers were more likely to access breast cancer prevention compared to non-smokers. Similarly, women who had undergone general prevention tests or had had a medical examination in the preceding four weeks for prevention or other reasons

or used CAM were more likely to undergo mammography. Women living in regions with high invitation coverage had a 100% higher probability of having had mammography when compared to women living in regions with low invitation coverage.

The effect of socioeconomic variables was similar in all the regions, regardless of invitation coverage levels. Residual variability around the intercept was observed for both for Pap test and mammography (Figure 5), with a similar geographical pattern: southern regions (except for Abruzzo, Apulia and Sardinia) showed a significantly higher probability of underuse of screening tests.

Discussion

Differences between geographical areas

Taking into account differences between the different Italian geographical areas, the observed national screening test uptake was 62.1% for cervical cancer and 56.4% for breast cancer. These values are lower than the Italian and the European guidelines reference standards for screening programmes: 70% acceptable and 85% desired for cervical cancer and 70% acceptable and 75% desired for breast. [2,4,21] Strong uptake differences still exist between regions, with a clear north-south gradient.[8] A positive trend is that differences between northern and southern Italy have diminished compared with the previous NHIS surveys due to increased coverage/access in the southern regions.[16] Differences between regions can be largely attributed to the NHS's ability to offer screening programmes that reach the target population. This hypothesis is also supported by the results of multilevel models showing how variability between regions is strongly related to screening programme coverage in the single regions, particularly for mammography. This phenomenon can be observed at a macrolevel: those regions with higher uptake are also those with higher access in the frameworks of screening programmes or of the NHS. The effect on total uptake of organized screening with active invitations to the target population is well known and has been observed in all contexts.[22,10,23] Finally, it is also interesting to note that total and screening programme uptake patterns are similar in almost all regions. This suggests that where the population's attention to prevention is low, there has also been difficulty in implementing screening programmes. This result is consistent with the consolidated evidence of an association between low/changeable invitation coverage of screening programmes and low response from the population to invitations.[5,6,19,20]

It is not easy to understand the causal relationship; if a context is unfavourable to the organisation of complex and multidisciplinary paths, is this because the population in that context does not trust

the NHS and thus does not respond to the invitation? Or is it because the poor organisation directly penalises compliance with programme recommendations?

Socioeconomic differences

Socioeconomic differences in uptake are still very evident, whichever variable is considered: education, citizenship, occupation or perceived economic difficulties. In particular, foreign women had a 40% lower uptake probability than Italians for Pap test and 55% lower probability for mammography. In Italy, immigration is a recent phenomenon, with a marked increase during the first decade of the 2000s, so it is conceivable that both cultural and language barriers may influence access to screening programmes and health services. However, a recent paper showed that screening uptake was heterogeneous by area of origin (Africans have lower Pap test and mammography uptake) and by region of residence,[24] highlighting that there are margins for improving equity. Regarding education, our result confirms what has been observed in England,[25] where a recent study showed a significant improvement of equitable delivery of breast screening but not of cervical screening.[26] Unfortunately, our dataset did not include information on income, though we can show the effect of economic conditions indirectly through survey respondents' perceived economic difficulties. Nevertheless, its association with uptake is more difficult to interpret, as this variable combines objective available resources and factors related to more subjective perception of precarious conditions or worsening of one's economic situation.[27] These latter factors are more related to personal coping - the ability to react to changes and difficulties, a personal characteristic known to be associated with participation in screening; "maladaptive coping", instead, is associated with poor compliance with cancer screening recommendations.[15] These personal characteristics are difficult to modify through active interventions such as invitation letters or information campaigns.[27,28]

Even though organized screening programmes and the NHS guarantee wider and easier access to screening, thus increasing coverage in all contexts, surprisingly, no reduction in socioeconomic differences was observed in the areas where screening programmes had higher invitation coverage. This effect on reducing access inequalities has been observed in other Italian studies.[12,29] Furthermore, the implementation of screening programmes has shown a levelling effect on breast cancer outcomes, with women in the lowest socioeconomic level attaining the same survival rates as those in the highest socioeconomic level.[30,31]A decrease in inequalities in access to effective prevention measures thanks to screening programmes and to the NHS actively promoting interventions has been observed in a number of other studies,[6,10,32,33] even though considerable exceptions or failures have also been observed.[34,35,36]

Association with other preventive health behaviours

We observed associations between screening uptake and single preventive health behaviours in organised programs and in public in private opportunistic setting. The existing synergy between prevention interventions and preventive health behaviours is a well-known phenomenon which offers the NHS opportunities to promote coordinated prevention initiatives.[37]

The association between both screening test uptake and being a former smoker is not surprising and has been reported by other authors;[38,39] instead, a slightly higher uptake for both Pap test and mammography in current smokers than in non-smokers is more surprising. It should be noted that the prevalence of smoking in Italy is higher among the highly educated; the difference in screening uptake thus almost disappears when adjusting for educational level. Particular attention should be paid to the association between mammography uptake and use of CAM, a partially unexpected result, as breast screening has been criticized in the last few years by groups concerned with overdiagnosis and overtreatment and against the medicalisation of the healthy population.[40,41] These opinions, which are not against technology per se, are welcome in cultural contexts that refuse a technological approach to life and health care and that are often attracted to CAM.[42] A positive association between CAM and mammography coverage thus suggests that a lack of coverage is, to a large degree, not a conscious choice but instead due to the lack of access to the service.

Limitations and strengths of the study and comparison with other data

The main limitations of the data used in the present study are related to data collection techniques, namely a retrospective study based on the recall of the interviewed women. When recalling past events, it can be difficult to distinguish between different organizational and administrative ways of how the test was delivered. For example, a test undergone in the framework of a screening programme could be confused with a test provided by the NHS outside an organised programme (in some local health services, the patient cannot perceive this difference). This observation does not influence total uptake but can generate incorrect classification of access modalities that can differ between Italian women and foreign nationals or between different educational levels. In fact, it can be difficult to define just what a "screening programme" is, resulting in a possible misunderstanding and thus confusing it with a more general access to a public health centre, particularly by less educated women or foreigner nationals with linguistic barriers. For this reason, most of the analysis was conducted by using the two indicators "public sector uptake" and "screening programme uptake" to give an idea of the range of the actual data. Furthermore, some women undergo tests at shorter intervals than is recommended,[6,43] which can mask part of the uptake obtained by the NHS

when we look at the most recent test only, as in this survey. In fact, if a woman has already undergone a test performed in the NHS and then undergoes an opportunistic test before the recommended interval has expired, she will register as covered by the opportunistic test and not by the previous NHS test. Thus, we underestimate the coverage by the public sector, which adopts less intensive protocols and longer intervals.[43,27,44] Furthermore, a survey with less stringent questions to identify the date of the last screening test may overestimate coverage due to telescoping effect (women reporting having undergone the test more recently than in fact they have), as noted in a previous Italian survey.[44] Indeed, the questions about the last screening test are posed slightly differently in the Italian NHIS and in the routine surveillance system – the PASSI survey – managed by the local health authorities.[34] This surveillance reports an overall uptake of 77% and 70% for cervical and breast cancer screening, respectively. It is also important to underline that the HPV test, which was authorized as a primary screening test instead of the Pap test in women older than 30-35 years in January 2013 by the Italian Ministry of Health, was available only through some pilot projects until 2014. Given that the NHIS interviews were conducted in 2012-2013 and that the questions referred to tests undergone in the three preceding years, obviously very few women had been invited to HPV screening at that point.[19,29,44] Among the strengths of this study to be mentioned is the enormous information potential of the Istat survey, both at the individual and at the family level, offering a very rich description of individual women, their families and their socioeconomic status. Unfortunately, for this study, we had access to a restricted dataset of the NHIS. Therefore the association between screening uptake and some potentially relevant information, as the family composition or the citizenship of the partner, could not be studied.

Another strong point is the inclusion of an ecological variable on the screening offered from a second data source. The joint use of these two data sources made it possible to estimate the impact of screening programmes on overall screening uptake and on differences in screening uptake between regions taking into account different socioeconomic and behavioural characteristics.

Conclusions

Total coverage observed through the Italian NHIS is below the desired and acceptable levels recommended by the European Commission.

Screening programmes increase uptake and have the potential, when correctly implemented, to decrease geographical inequalities, although not those differences caused by individual attitudes towards health and prevention.

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Contributors

AP, PGR and LG designed and initiated the study and wrote the manuscript. LF extracted the data, conducted statistical analysis, interpreted the findings and reviewed/edited the manuscript. BG conducted statistical analysis. ADN reviewed and edited the manuscript. MZ and CM contributed to the discussion and critically reviewed the final manuscript. All authors read and approved the final manuscript.

Data sharing statement

The analyses were performed using data based on Istat's surveys. In particular, we used Istat's standard files (issued upon request with a valid reason for research purposes and released free of charge and in compliance with the principle of statistical secrecy and protection of personal data). To acquire such files, it is necessary to register in the area of the Istat website dedicated to data use and to accept the terms of use. Data are available in different formats (TXT, STATA, SAS, R).

Competing interests

None declared

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References

1. Osservatorio Nazionale Screening. 2014. I programmi di screening in Italia. http://www.osservatorionazionalescreening.it/sites/default/files/allegati/Screening_2014_web.pdf
2. Giorgi D, Giordano L, Ventura L, et al. Mammography breast cancer screening in Italy: 2010 survey. *Epidemiol Prev* 2012;361:8–27.
3. von Karsa L, Anttila A, Ronco G, et al., eds. Cancer screening in the European Union. Report on the implementation of the Council Recommendation on cancer screening. First report. Luxembourg: European Commission, 2008.
4. Perry N, Broeders M, de Wolf C, et al., eds. European guidelines for quality assurance in breast cancer screening and diagnosis. Luxembourg: European Commission. Office for Official Publications of the European Communities, 2006.
5. Zappa M, Carozzi FM, Giordano L, et al. The diffusion of screening programmes in Italy, years 2011-2012. *Epidemiol Prev* 2015;39:5–8.
6. Giorgi Rossi P, Camilloni L, Cogo C, et al. [Methods to increase participation in cancer screening programmes]. *Epidemiol Prev* 2012;36:1–104.
7. ISTAT. La prevenzione dei tumori femminili in Italia il ricorso a Pap test e mammografia. Anni 2004-2005. Roma, 2006.
8. Giorgi Rossi P, Carrozzi G, Federici A, et al. Invitation coverage and participation in Italian cervical, breast and colorectal cancer screening programmes. *J Med Screen* 2017;Jan1. doi: 10.1177/0969141317704476.
9. Green LW and Kreuter MW. Health program planning: an educational and ecological approach. 4th ed. New York: McGraw-Hill, 2005.
10. Palència L, Espelt A, Rodríguez-Sanz M, et al. Socio-economic inequalities in breast and cervical cancer screening practices in Europe: influence of the type of screening program. *Int J Epidemiol* 2010;39:757–65. doi: 10.1093/ije/dyq003.
11. Jepson R, Clegg A, Forbes C, Lewis R, Sowden A, Kleijnen J. The determinants of screening uptake and interventions for increasing uptake: a systematic review. Health Technol Assess. 2000;4(14):i-vii, 1-133.
12. Labeit, A., Peinemann, F., Baker, R., 2013. Utilisation of preventative health check-ups in the UK: findings from individual-level repeated cross-sectional data from 1992 to 2008. BMJ Open 3, e003387. doi:10.1136/bmjopen-2013-003387
13. Zappa, M., Castiglione, G., Giorgi, D., Grazzini, G., Paci, E., Ciatto, S., 1998. Re: Participation in colorectal cancer screening: a review. J. Natl. Cancer Inst. 90, 465.
14. Wools, A., Dapper, E.A., Leeuw, J.R.J. de, 2016. Colorectal cancer screening participation: a

systematic review. Eur. J. Public Health 26, 158–168. doi:10.1093/eurpub/ckv148

15. Douglas E, Waller J, Duffy SW, Wardle J. Socioeconomic inequalities in breast and cervical screening coverage in England: are we closing the gap? J Med Screen. 2016 Jun;23(2):98-103. doi: 10.1177/0969141315600192.
16. ISTAT. 2006. Fattori di rischio e tutela della salute — Indagine multiscopo sulle famiglie italiane "Prevenzione dei tumori femminili: ricorso a pap test e mammografia" anni 2004/2005. http://www3.istat.it/salastampa/comunicati/non_calendario/20061204_00/testointegrale.pdf
17. ISTAT. 2013. Multiscopo sulle famiglie: condizioni di salute e ricorso ai servizi sanitari. http://siqual.istat.it/SIQual/visualizza.do?id=0071201
18. Ronco G, Giorgi Rossi P, Giubilato P, et al. A first survey of HPV-based screening in routine cervical cancer screening in Italy. *Epidemiol Prev* 2015;39:77–83.
19. Ronco G, Giubilato P, Carozzi F, et al. Extension of organized cervical cancer screening programmes in Italy and their process indicators, 2011-2012 activity. *Epidemiol Prev* 2015;39:61–76.
20. Ventura L, Giorgi D, Giordano L, et al. Mammographic breast cancer screening in Italy: 2011-2012 survey. *Epidemiol Prev* 2015;39:21–9.
21. Anttila A, Ronco G, Nicula F, et al. Organization of cytology-based and HPV-based cervical cancer screening. In: Anttila A, Arbyn M, De Vuyst H, et al., eds. European guidelines for quality assurance in cervical cancer screening. Luxembourg: Publications Office of the European Union, 2015, Second edition – supplements: pp. 69–108.
22. Nygård JF, Skare GB, Thoresen SØ. The cervical cancer screening programme in Norway, 1992-2000: changes in Pap smear coverage and incidence of cervical cancer. *Med Screen* 2002;9(2):86-91.
23. Ferroni E, Camilloni L, Jimenez B, et al. How to increase uptake in oncologic screening: a systematic review of studies comparing population-based screening programs and spontaneous access. *Prev Med* 2012;55:587–96. doi: 10.1016/j.ypmed.2012.10.007.
24. Francovich L, Di Napoli A, Giorgi Rossi P, Gargiulo L, Giordani B, Petrelli A. [Cervical and breast cancer screening among immigrant women resident in Italy]. Epidemiol Prev. 2017 May-Aug;41(3-4 (Suppl 1)):18-25. doi: 10.19191/EP17.3-4S1.P018.061. Italian.
25. Sabates R, Feinstein L. The role of education in the uptake of preventative health care: the case of cervical screening in Britain. Soc Sci Med. 2006 Jun;62(12):2998-3010.
26. Sabates R, Feinstein L. Do income effects mask social and behavioural factors when looking at universal health care provision? Int J Public Health. 2008;53(1):23-30. PubMed PMID: 18522366.

27. Federici A, Guarino A, Serantoni G. Adesione ai programmi di screening di prevenzione oncologica: proposta di una modellizzazione dei risultati di revisione della letteratura secondo il Modello PRECEDE-PROCEED. *Epidemiol Prev* 2012;36:1–104.
28. Federici A, Poletti P, Guarino A, et al. Garantire la partecipazione consapevole. In: Federici A, ed. Screening - Profilo complesso di assistenza. Roma: Il Pensiero Scientifico, 2007: pp. 252–257.
29. Carrozzi G, Sampaolo L, Bolognesi L, et al. Cancer screening uptake: association with individual characteristics, geographic distribution, and time trends in Italy. *Epidemiol Prev* 2015;39:9–18.
30. Pacelli B, Carretta E, Spadea T, et al. Does breast cancer screening level health inequalities out? A population-based study in an Italian region. *Eur J Public Health* 2014;24:280–5. doi: 10.1093/eurpub/ckt119.
31. Puliti D, Miccinesi G, Manneschi G, et al. Does an organised screening programme reduce the inequalities in breast cancer survival? *Ann Oncol* 2012;23:319–23. doi: 10.1093/annonc/mdr121.
32. Spadea T, Bellini S, Kunst A, et al. The impact of interventions to improve attendance in female cancer screening among lower socioeconomic groups: a review. *Prev Med* 2010;50:159–64. doi: 10.1016/j.ypmed.2010.01.007.
33. Giorgi Rossi P, Baldacchini F, Ronco G. The Possible Effects on Socio-Economic Inequalities of Introducing HPV Testing as Primary Test in Cervical Cancer Screening Programs. *Front Oncol* 2014;4:20. doi: 10.3389/fonc.2014.00020.
34. Lagerlund M, Bellocco R, Karlsson P, et al. Socio-economic factors and breast cancer survival - a population-based cohort study (Sweden). *Cancer Causes Control* 2005;16:419–30.
35. Louwman WJ, van de Poll-Franse LV, Fracheboud J, et al. Impact of a programme of mass mammography screening for breast cancer on socio-economic variation in survival: a population-based study. *Breast Cancer Res Treat* 2007;105:369–75.
36. Halmin M, Bellocco R, Lagerlund M, et al. Long-term inequalities in breast cancer survival--a ten year follow-up study of patients managed within a National Health Care System (Sweden). Acta Oncol 2008;47:216–224. doi: 10.1080/02841860701769768.
37. Bankhead CR, Brett J, Bukach C, et al. The impact of screening on future health-promoting behaviours and health beliefs: a systematic review. *Health Technol Assess* 2003;7:1–92.
38. Venkataraman K, Wee HL, Ng SHX, *et al.* Determinants of individuals' participation in integrated chronic disease screening in Singapore. *J Epidemiol Community Health* 2016;70:1242–50. doi:10.1136/jech-2016-207404

39. Labeit A, Peinemann F, Baker R. Utilisation of preventative health check-ups in the UK: findings from individual-level repeated cross-sectional data from 1992 to 2008. *BMJ Open* 2013;3:e003387. doi:10.1136/bmjopen-2013-003387
40. Grady D. Look for cancer, and find it! In: New York Times, 2014. http://well.blogs.nytimes.com/2014/04/07/look-for-cancer-and-find-it/
41. Gøtzsche PC, Hartling OJ, Nielsen M, Brodersen J, Jørgensen KJ. Breast screening: the facts--or maybe not. BMJ 2009;338:b86–b86. doi: 10.1136/bmj.b86.
42. Volpi R. L'amara medicina. Come la sanità italiana ha sbagliato strada. Milano: Feltrinelli, 2008.
43. Ronco G, Segnan N, Giordano L, et al. Interaction of spontaneous and organised screening for cervical cancer in Turin, Italy. *Eur J Cancer* 1997;33:1262–7.
44. Giorgi Rossi P, Esposito G, Brezzi S, et al. Estimation of Pap-test coverage in an area with an organised screening program: challenges for survey methods. *BMC Health Serv Res* 2006;6:36.

Box 1. Characteristics of the Italian organized screening programmes in 2013.

	Cervical cancer screening	Breast Cancer Screening
Target age	25-64	50-69 [a]
Test	Pap test [b]	Mammography (double projection)
Interval	3 years	2 years
Proportion of the target population regularly invited	70.8%	73.9%
Participation rate	40.9%	57.0%

[a] In two regions, Emilia-Romagna and Piedmont, the target age was extended in 2010 to ages 45-74. In these regions the screening interval is one year for women aged 45-49.

[b] Since January 2013, the Italian Ministry of Health now recommends HPV-DNA test, followed by cytology triage in case of HPV positivity, with 5-year interval, as an alternative option to Pap test every three years for women >=30. When the interviews was conducted in 2013, only few pilot studies used HPV as primary screening test, accounting for 7.5% and 6.9% of the invited population in 2012 and 2013, respectively.

Table 1. Pap test and mammography: total uptake, uptake in the National Health Service and public screening coverage, by educational level, occupation, and perception of economic family resources. Italy, 2012-2013.

	PAP TEST (n=32,831)			MAMMOGRAPHY (n=16,459)		
		uptake in the NHS			uptake in the NHS	
	Total uptake	Of which public screening coverage	Total	Total uptake	Of which public screening coverage	Total
Age						
25-29	48.5	13.3	28.2			
30-34	58.1	18.6	35.7			
35-39	63.8	19. 9	37.3			
40-44	65.1	21.9	38.2			
45-49	72.1	23.6	42.8			
50-54	69.1	26.6	45.2	60.5	28.1	44.9
55-59	60.2	25.9	41.4	57.7	29.8	44.4
60-64	53.3	25.7	39.1	55.4	32.2	44.8
65-69				50.7	29.4	41.6
Citizenship						
Italian	63.2	26,0	37.4*	55.9	30.7	44.2
Foreign national	52.2	23.8	40.6	41.4	20.9	32.4
Educational level						
Degree	68.6	20.2	37.2	65.5	29.9*	46.5
School-leaving certificate	64.6	21.5	37.4	60.8	28.8	44.3
Compulsory education	57.8	23.6	40.8	53.3	30.2	43.5
Occupation						
Executive, Entrepreneur, Freelance professional	74.4	20.1	35.4	65.1	27.8	40.9
Office worker	73,0	23.9	40.4	68.1	33.1	49.7
Workman, Apprentice, Other	64.1	28.2	45.8	58.2	34.6	48.6
Independent businessman, Homecare assistant, Cooperative member	67.5	24.7	40.2	60.5	35.7	50.4
Contract worker	60.2	20.3	34.4	59.9	21.3	40.4
Not employed	54.1	19.5	36.3	52.8	28.3	41.9
Perceived economic resources						
Excellent/Adequate	66.0	25.6	41.8	60.9	32.4	46.9
Scarce/Insufficient	53.9	21.9	38.8	48.6	25.4	39.2
Reasons hampering pursuit of hobbies or interests						
Other	60.3	22.0	38.7	55.4	29.5	43.3
Too busy	67.6	22.9	39.5	61.1	31.3	47.7
Smoking habits						
Smoker	62.2	21.9	38.6	56.6	30.9	45,0
Former smoker	70.9	26.8	43.8	63.8	35.2	51.3
Non-smoker	59.6	21.1	37.6	53.8	27.7	41.3
Physical activity						
No	55.9	19.4	36.2	47.7	24,0	37.3

Yes	67.9	24.8	41.4	64.9	35.5	50.6
Weight control						
Rarely or never	56.9	20.7	36.1	48.7	25.2	37.7
Weight controlled	65.2	23.1	40.6	61.4	32.9	48.2
Preventive medical examinations in the preceding 4 weeks						
No examination	58.0	20.9	37,0	52.2	28.2	41,0
At least one preventive examination	75.0	23.7	41.8	65.8	32.9	49.5
Examinations for other reasons	68.7	25.5	43.4	61.8	32.1	48.5
General prevention medical tests						
No test	43.7	16,0	28.5	35,0	18.9	27.2
1 or 2 tests	56.9	22.2	37.5	50.2	31.3	42.5
All tests	64.7	23,0	40.3	57.5	30.2	44.8
Use of complementary and alternative medicine						
Never used or more than three years ago	60.0	21.3	38.2	54.9	29.1	43,0
At least once in the last three years	79.2	29.6	44.8	68.5	35.9	52.2
Total	**62.1**	**22.2**	**38.9**	**56.4**	**29.8**	**44,0**

All differences are statistically significant, except *

Table 2. Multilevel logistic random intercept model for Pap test. Model on having had the test in the three years prior to interview. Italy, 2012-2013.

Variable		Adjusted OR	95% CI	
Individual				
Age group	25-34	1		
	35-44	1.45	1.33	1.56
	45-54	1.89	1.75	2.04
	55-64	0.99	0.92	1.08
Citizenship	Foreign national	1		
	Italian	1.69	1.54	1.85
Educational level	Compulsory education	1		
	School-leaving certificate	1.12	1.05	1.19
	Degree	1.16	1.08	1.27
Perceived economic resources	Scarce, Absolutely insufficient	1		
	Excellent, adequate	1.25	1.18	1.32
Occupation	Unemployed	1		
	Executive, Entrepreneur, Freelance professional	1.08	0.87	1.32
	Office worker	1.35	1.16	1.54
	Workman, Apprentice, Other	1.18	1.05	1.32
	Independent businessman, Homecare assistant, Cooperative member	1.15	1.06	1.23
	Contract worker	1.28	1.19	1.37
Reasons hampering pursuit of hobbies or interests	Other reasons	1		
	Too busy	1.19	1.12	1.27
Smoking habits	Non-smoker	1		
	Former smoker	1.37	1.28	1.45
	Smoker	1.08	1.01	1.15
Physical activity	No	1		
	Yes	1.16	1.10	1.22
Weight control	Rarely or never	1		
	Periodically	1.25	1.19	1.32
Preventive medical examinations in the preceding 4 weeks	No examination	1		
	Other reasons	1.43	1.33	1.52
	Preventive examination	1.75	1.59	1.92
General prevention medical tests	No test	1		
	1 or 2 tests	1.41	1.25	1.61

	All tests	1.85	1.72	2.00
Use of complementary and alternative medicine	Never used or more than three years ago	1		
	At least once in the last three years	1.41	1.30	1.54
Contextual				
Invitation coverage in the period 2011-13	Within the median	1		
	above the median	2.12	1.43	3.13
Random effect				
		Estimate	**Standard error**	**P-value**
$\alpha_{i,\ regions}$		0.209	0.066	<0.01
ICC - Intraclass Correlation Coefficient (ρ)		0.06		

Table 3. Multilevel logistic random intercept model for mammography. Model on having had mammography in the two years before interview. Italy, 2012-2013.

Variable		Adjusted OR	95% CI	
Individual				
Age group	50-59	1		
	60-69	0.75	0.69	0.81
Citizenship	Foreign national	1		
	Italian	2.22	1.85	2.70
Educational level	Compulsory education	1		
	School-leaving certificate	1.09	0.99	1.18
	Degree	1.30	1.14	1.47
Perceived economic resources	Scarce, Absolutely insufficient	1		
	Excellent, adequate	1.23	1.15	1.33
Occupation	Unemployed	1		
	Executive, Entrepreneur, Freelance professional	1.47	0.94	2.27
	Office worker	0.99	0.79	1.25
	Workman, Apprentice, Other	1.02	0.86	1.20
	Independent businessman, Homecare assistant, Cooperative member	1.10	0.97	1.25
	Contract worker	1.23	1.10	1.37
Reasons hampering pursuit of hobbies or interests	Other reasons	1		
	Too busy	1.15	1.04	1.25
Smoking habits	Non-smoker	1		
	Former smoker	1.18	1.09	1.28
	Smoker	1.00	0.92	1.10
Physical activity	No	1		
	Yes	1.37	1.28	1.47
Weight control	Rarely or never	1		
	Periodically	1.33	1.25	1.43
Preventive medical examinations in the last 4 weeks	No examination	1		
	Other reasons	1.52	1.41	1.64
	Preventive examination	1.56	1.41	1.75
General prevention medical tests	No test	1		
	1 or 2 tests	1.43	1.12	1.82
	All tests	2.00	1.69	2.38

Use of complementary and alternative medicine	Never used or more than three years ago	1		
	At least once in the last three years	1.22	1.09	1.37
Contextual				
Invitation coverage in the period 2011-13	Within the median	1		
	Above the median	2.00	1.43	2.78
Random effect				
		Estimate	**Standard error**	**P-value**
$\alpha_{i,\ regions}$		0.136	0.045	<0.01
ICC- Intraclass Correlation Coefficient (ρ)		0.04		

Figure legends

Figure 1. Utilization of Pap test (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

Figure 2. Utilization of Pap test (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

Figure 3. Utilization of mammography (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

Figure 4. Utilization of mammography (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

Figure 5. Level 2 residuals of hierarchical models for Pap test and mammography. Italy, 2012-2013.

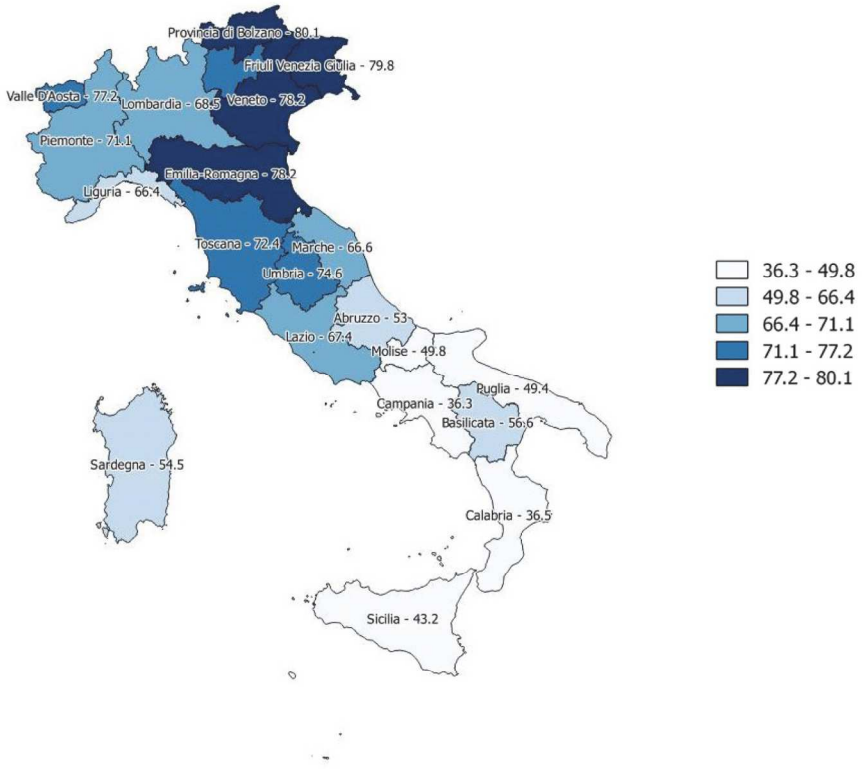

Figure 1. Utilization of Pap test (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

160x126mm (300 x 300 DPI)

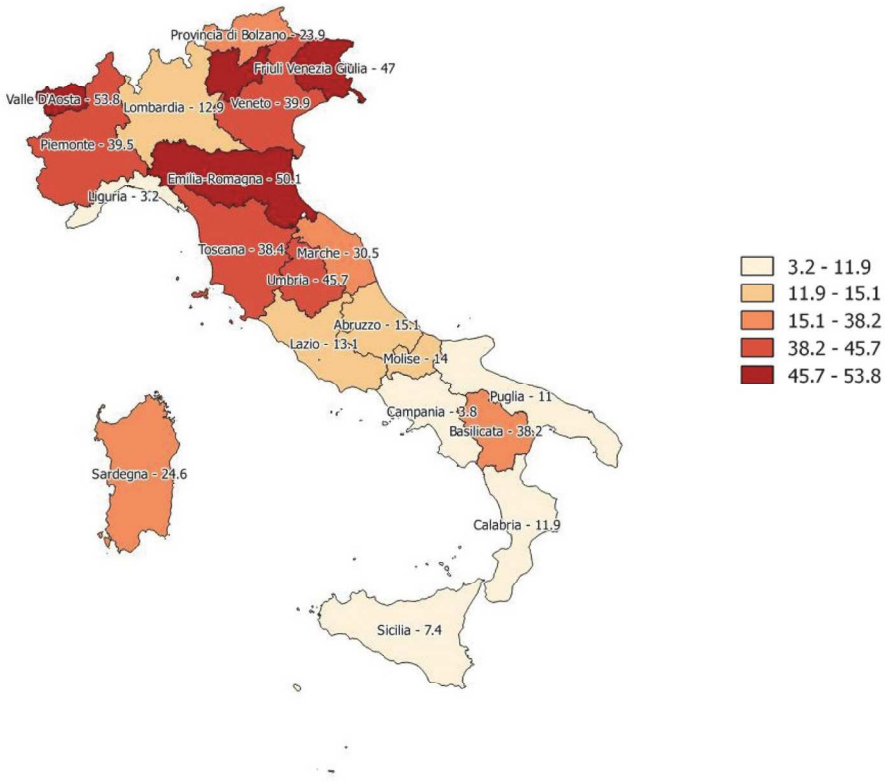

Figure 2. Utilization of Pap test (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

157x125mm (300 x 300 DPI)

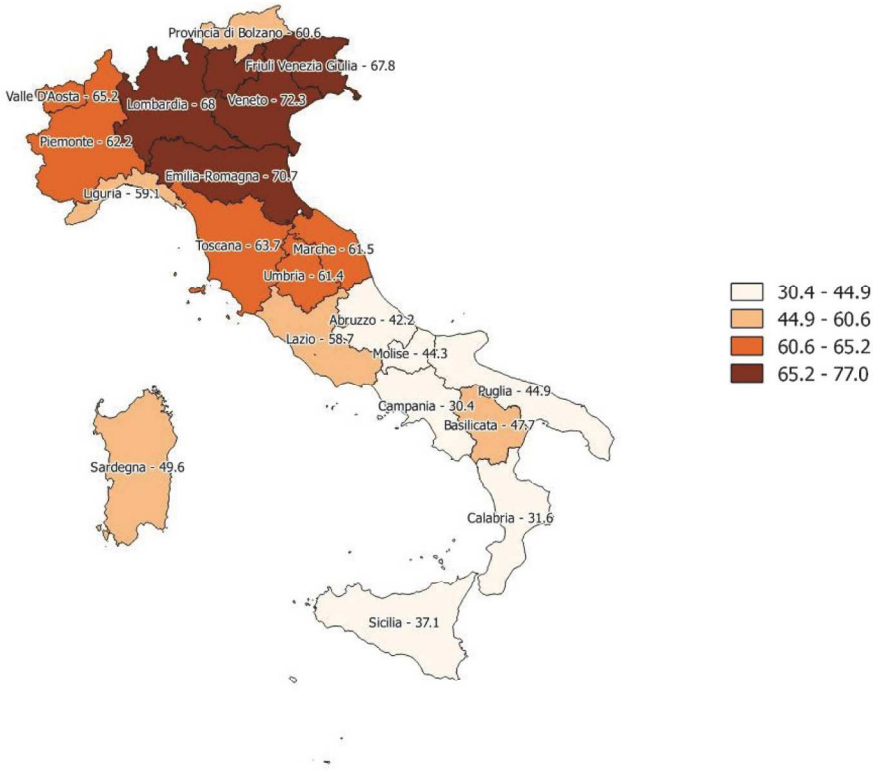

Figure 3. Utilization of mammography (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

159x124mm (300 x 300 DPI)

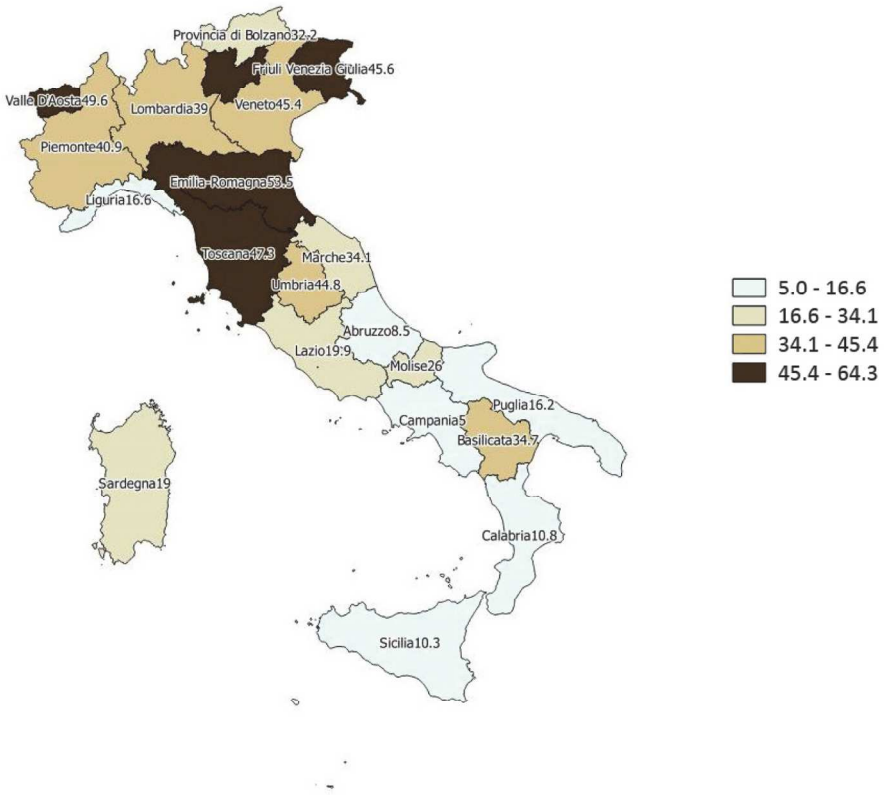

Figure 4. Utilization of mammography (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

154x125mm (300 x 300 DPI)

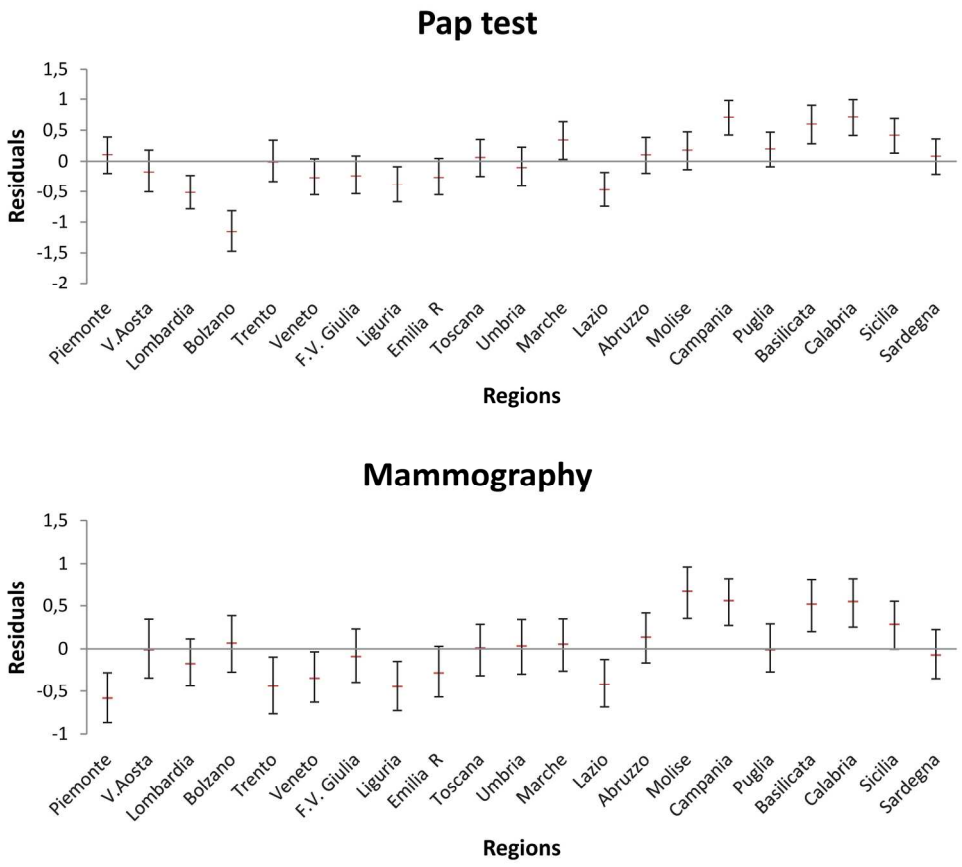

Figure 5. Level 2 residuals of hierarchical models for Pap test and mammography. Italy, 2012-2013.

175x158mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods	

taking account of sampling strategy

(*e*) Describe any sensitivity analyses

Continued on next page

Results			**Page number**
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	6-7
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-8
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Geographic and socioeconomic differences in uptake of Pap test and mammography in Italy: results from the National Health Interview Survey

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology, Health services research, Oncology
Keywords:	Pap test, mammography, socioeconomic, immigrants, geographic, Italy

Title

Geographic and socioeconomic differences in uptake of Pap test and mammography in Italy: results from the National Health Interview Survey

Short title

Factors associated with Pap test and mammography uptake

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Number of figures: 5

Abstract

Objective: The Italian National Health Service (NHS) instituted cervical and breast cancer screening programmes in 1999; the local health authorities have a mandate to implement these screening programmes by inviting all women aged 25-64 for a Pap test every three years (or for an HPV test every five years) and women aged 50-69 for a mammography every two years. However, the implementation of screening programmes throughout the country is still incomplete. The study aims to: 1) describe cervical and breast cancer screening uptake; 2) evaluate geographic and individual socioeconomic difference in screening uptake.

Methods: Data both from the Italian National Health Interview Survey (NHIS) conducted by the National Institute of Statistics (Istat) in 2012-2013 and from the Italian National Centre for Screening Monitoring (INCSM) were used. The NHIS interviewed a national representative random sample of 32,831 women aged 25-64 and of 16,459 women aged 50-69. Logistic multilevel models were used to estimate the effect of socioeconomic variables and behavioural factors (level 1) on screening uptake. Data on screening invitation coverage at the regional level, taken from INCSM, were used as ecological (level 2) covariates.

Results: Total three-year Pap test and two-year mammography uptake was 62.1% and 56.4%, respectively; screening programmes accounted for 1/3 and 1/2 of total test uptake, respectively. Strong geographical differences were observed. Uptake was associated with high educational levels, healthy behaviours, being a former smoker, and being Italian vs. foreign national. Differences in uptake between Italian regions were mostly explained by the invitation coverage to screening programmes.

Conclusions: The uptake of both screening programmes in Italy is still under acceptable levels. Screening programme implementation has the potential to reduce the health inequalities gap between regions but only if uptake increases.

Keywords: Pap test, mammography, socioeconomic, immigrants, geographic, Italy

Strengths and limitations of this study

- The large amount of information derived from NHIS survey allowed us to investigate inequities in screening uptake in Italy thoroughly for the first time.
- The joint use of two data sources enabled estimating the impact of screening programmes on uptake in the country, evaluating also the differences between regions, and in groups with different socioeconomic and behavioural characteristics.
- The collection of data based on the recall of the interviewed women can make it difficult to distinguish how the test was delivered (screening programme or opportunistic) in a potentially differential way by citizenship or between different educational levels.
- The uptake obtained by the public sector, which adopts less intensive protocols and longer intervals, may be underestimated, looking at the most recent test only, because some women undergo tests at shorter intervals than recommended.

Introduction

As cervical and breast cancer screening programmes have proven effective in reducing morbidity and mortality, the European Commission recommended in 2003 that each EU Member State offer screening to its population. In accordance with these recommendations, population-based free screening programmes, with active invitation of the target population as well as quality assurance and monitoring activities, are included in the essential health care services guaranteed by the Italian National Health Service (NHS). The target population for cervical screening includes all permanent and temporary (when possible) resident women aged 25-64, and for breast screening, women aged 50-69;[1,2] the screening tests used are a Pap test every three years and mammography every two years, in accordance with EU Recommendations (see box 1).[3,4]

The introduction of screening programmes in Italy has been slow and characterized by profound geographical differences. The difficulties and delays in organized screening activation have favoured the spread of opportunistic screening, both by public and private providers.[5] Thus, actual screening coverage and uptake is the result of both organized and opportunistic screening models.[6] Organized public screening programmes include a monitoring system to determine exactly how many women are invited and screened in the target population, while opportunistic screening tests are registered in a way that does not allow a calculation of test coverage, and some are not registered at all.[6] Thus, the only way to have complete information about screening coverage is by interviewing the target population. The spread of opportunistic testing and the progressive implementation of organized screening has led to a marked increase in test coverage. In 1994, the once-in-a-lifetime Pap test (ages 25-64) uptake was 60% and mammography (ages 50-69) uptake was 44%, virtually all due to opportunistic screening. In 2004, both tests had an uptake of 71%, with organised screening playing a major role, particularly for mammography. [7] Nevertheless, the role of the two models in maintaining high test uptake now in Italy is unclear, and a previous project, [8] based on the Green and Kreuter model[9] demonstrated a negative association between organized and opportunistic screening. In the same project, factors have been classified as predisposing (scarcely or not modifiable, as age, socio-economic status, coping and other preventive behaviours), reinforcing (for example knowledge of the disease and of the screening effect, supporting network, i.e. modifiable factors acting on the target population) and enabling factors (for example accessibility and visibility of the screening services, i.e. modifiable environmental factors). Public health interventions, both health promotion and organization of health service, can modify the behaviours and make the environment more favourable through modification of reinforcing and enabling factors.[10]

In this model, organized programmes are supposed to be effect modifiers of the association between socioeconomic factors and screening participation, reducing inequalities, because the access to opportunistic screening is more probable among affluent people. In fact, organized programmes have shown to reduce inequality in access, particularly for mammography.[11] Furthermore, studies on the association between healthy behaviours and screening uptake have shown inconsistent results;[12] the heterogeneity could be due to the different screening settings, with organized programmes showing no or small differences,[13] particularly in colorectal cancer screening.[14,15] In Italy, the coexistence of opportunistic and organized screening and the wide variation among regions in the level of organised screening implementation makes it possible to study how these two ways of delivering screening interact with the known determinants of screening uptake.

Study objectives are: 1) to describe cervical and breast cancer screening uptake in Italy based on data from the Italian National Health Interview Survey (NHIS) conducted by National Institute of Statistics (Istat) in 2012-2013. We distinguish overall uptake and uptake within organised screening programmes; 2) study geographic and individual socioeconomic difference in screening uptake, and the impact of screening programme invitation coverage on these determinants.

Methods

Data sources

This study is part of epidemiological and political analyses of the barriers to implementation of and participation in screening programmes in Italy conducted within the framework of the Green and Kreuter model.[9,10,16]

The study was conducted based on data from the NHIS, a population-based cross-sectional survey conducted every five years in Italy by the Istat[17,18] and from the Italian National Centre for Screening Monitoring (INCSM). The 2012-2013 edition of the NHIS collected information about screening coverage and investigated the characteristics of women who availed themselves of female cancer screening programmes, as well as other social, healthcare and behavioural covariates.

Thanks to funding from the Italian National Health Fund, the survey sample was enlarged in the 2013 survey edition, and an in-depth analysis of results from each Region was performed.

It was hypothesized that total uptake is also influenced by accessible, free screening services. Thus, a variable measuring the proportion of the target population invited by the screening programme within the correct interval (the invitation coverage) at the regional level (ecological variable) was created based on data from the INCSM.[12,19,20,21] The intervals considered were 3 years for Pap test and 2 years for mammography.

Patient and Public Involvement

No patients neither healthy individuals were involved for this study.

Outcomes

Cervical screening uptake is defined as the percentage of women in the target age group (aged 25-64) who received at least one Pap test in the three years prior to the interview (n=32,831, representing the population of 16,752,400 women in Italy). Breast cancer screening uptake is defined as the percentage of women in the target age group (aged 50-69) who underwent at least one mammography in the two years prior to the interview (n=16,459, representing a population of 7,925,570 women in Italy).

Three uptake indicators were identified, based on the responses to the NHIS questionnaire: 1) total uptake, including services delivered in all types of healthcare facilities (public or private) and performed upon invitation of public screening programme, on suggestion of general practitioner or private doctor or on own initiative); 2) uptake in a public healthcare facility, upon the suggestion of a general practitioner or private doctor or on own initiative; 3) uptake in a public healthcare facility, upon invitation to public screening programme.

Definition of individual and context factors and data analysis

A descriptive analysis evaluated the distribution of the three above-mentioned uptake indicators combined with the following fundamental dimensions: region of residence, age, citizenship, educational level, occupation, perception of economic resources, reasons hampering the pursuit of hobbies and interests (considered a proxy of availability of time), smoking habits, physical activity, weight control frequency, preventive medical examinations in the four weeks prior to the interview, general prevention tests (cholesterol, glycaemia, blood pressure) in the four weeks prior to the interview and use of complementary and alternative medicine (CAM). Regarding preventive medical examinations, we classified the variable in three categories, based on the answers to the questionnaire: 1) no examination, 2) at least one preventive examination (in the absence of disorders or symptoms), 3) examinations for other reasons (diseases or disorders, prescriptions, medical certificates, other). Hierarchical logistic models, adjusted for all the above-mentioned covariates, were tested to evaluate geographic and socioeconomic differences in Pap test and mammography uptake. The first-level unit was all target women and the second level unit was the Italian Regions (21 units). Hierarchical models were used because it can be hypothesized that Pap test and mammography uptakes have a structure of correlation between individuals that differs between regions of residence both for the effect of the heterogeneity of the public screening

programme organization and for the homogeneity in the population's socioeconomic and demographic characteristics within each region. We estimated the geographical differences as regional residual around level 1 intercept, which can be interpreted as the national mean effect after adjustment for all the covariates considered. We also calculated the intra-class correlation coefficient (ICC) for the null model (without covariates), which represents the proportion of variability that can be attributed to differences between the regions. The effect of socioeconomic level was evaluated by the estimation of the odds ratios (OR) related to citizenship, educational level, perception of economic resources and occupation.

Having had a Pap test in the three years prior to the interview (two years for mammography) was used as outcome variable based on tests performed in screening programmes and in opportunistic settings, both public and private. The above-listed categorical variables were included as first-level covariates.

Finally, in order to evaluate possible associations between the level of organised screening offered and socioeconomic access inequalities, the interaction between invitation coverage and educational level and between invitation coverage and perceived economic resources were tested. Invitation coverage was calculated as the number of invitations sent by the organised screening programme in 2011-2013 for the Pap test and in 2010-2011 for mammography divided by the total target population for each screening programme as reported by the Istat. The regional invitation coverage variable was divided into two categories based on the distribution median; Pap test cut-off was 63% and mammography cut-off was 77%.

Results

Total Pap test uptake was slightly under two-thirds of the total target group (61.1%), 38.9% in the NHS and 22.2% in public screening programmes.

Total uptake ranged from 36.6% in Campania to 79.8% in Friuli-Venezia Giulia (Figure 1), while in screening programmes it ranged from 3.2% in Liguria to 53.8% in Valle d'Aosta (Figure 2). Total mammography uptake was seen in more than one-half of the target group (56.4%) and in 44.6% in the NHS, of which 29.8% was due to participation in public screening programmes. Total uptake ranged from 30.4% in Campania to 72.3% in Veneto (Figure 3), while screening programme uptake ranged from 5% in Campania to 64.3% in Trento (Figure 4).

The patterns of test uptake were very similar for Pap test and mammography in almost all regions. Total Pap test uptake increased with age up to 50 years (72.1%), and then decreased, while screening programme uptake did not decrease after age 50 (Table 1).

As regards mammography, no age differences were observed in uptake between the frameworks of screening programmes and of the NHS, although total coverage uptake did decrease with age.

Total Pap test and mammography uptake were higher among Italian women than foreign nationals. This difference for Pap test was larger in opportunistic screening than in screening programmes, while for mammography, a relevant gap in uptake between Italian and foreign nationals was observed also in screening programmes (30.7% vs. 20.9%).

A direct association between educational level and Pap test/mammography uptake was observed. Such an imbalance was due to lower uptake in opportunistic screening, primarily for mammography and exclusively for the Pap test.

In terms of occupation, Pap test total uptake progressively decreased from women with stronger and better paid working positions to those who lived in more unstable conditions and the unemployed. Executives, entrepreneurs, freelance professionals and office workers had higher uptake than other occupation categories, mostly due to higher uptake in private opportunistic screening. Unemployed women had low access to all screening modalities.

An association was observed between occupation and access/ uptake for mammography as well, particularly for total uptake. Perceived unsatisfactory economic resources were associated with lower total uptake, lower screening programme uptake and lower NHS uptake for both Pap test and mammography. Considering indicators related to attitude towards health and prevention, higher Pap test and mammography uptake was observed in women who had other preventive health behaviours such as preventive medical examinations in the preceding four weeks and general prevention tests, as well as more physical activity, better weight control and being a former smoker. Also, women who used CAM in the preceding three years had higher uptake.

Table 2 shows the results of the hierarchical logistic model for the probability of being screened for cervical cancer (i.e., Pap test in the three years prior to the interview) expressed as OR.

High educational level, adequate economic conditions (OR:1.25) and especially being Italian (OR:1.69) were factors associated with higher probability for having had a Pap test. Furthermore, women who declared that they had had any general prevention tests and/ or medical examinations, used any CAM and did any physical activity had higher probability of undergoing the Pap test in the recommended intervals. Finally, former smokers and current smokers were more likely to access cervical cancer prevention services than non-smokers.

Women living in regions with higher invitation coverage levels than the median had a higher probability of having the test than those women living in regions with lower invitation coverage levels (OR:2.12).

The effect of socioeconomic variables was similar in all the regions, regardless of invitation coverage levels.

As regards mammography, multivariate analysis (Table 3) confirms the results of the bivariate analysis: women aged 60-69 had a lower probability of having had a mammography in the years preceding the interview (OR:0.75). High educational level, adequate economic conditions (OR:1.23) and particularly being Italian (OR:2.22) were predisposing factors for accessing mammography. Furthermore, women who did any physical activity were more likely to have undergone mammography (OR:1.37). Former smokers were more likely to access breast cancer prevention compared to non-smokers. Similarly, women who had undergone general prevention tests or had had a medical examination in the preceding four weeks for prevention or other reasons or used CAM were more likely to undergo mammography. Women living in regions with high invitation coverage had a 100% higher probability of having had mammography when compared to women living in regions with low invitation coverage.

The effect of socioeconomic variables was similar in all the regions, regardless of invitation coverage levels. Residual variability around the intercept was observed for both for Pap test and mammography (Figure 5), with a similar geographical pattern: southern regions (except for Abruzzo, Apulia and Sardinia) showed a significantly higher probability of underuse of screening tests.

Discussion

Differences between geographical areas

Taking into account differences between the different Italian geographical areas, the observed national screening test uptake was 62.1% for cervical cancer and 56.4% for breast cancer. These values are lower than the Italian and the European guidelines reference standards for screening programmes: 70% acceptable and 85% desired for cervical cancer and 70% acceptable and 75% desired for breast. [2,4,22] Strong uptake differences still exist between regions, with a clear north-south gradient.[8] A positive trend is that differences between northern and southern Italy have diminished compared with the previous NHIS surveys due to increased coverage/access in the southern regions.[17] Differences between regions can be largely attributed to the NHS's ability to offer screening programmes that reach the target population. This hypothesis is also supported by the results of multilevel models showing how variability between regions is strongly related to screening programme coverage in the single regions, particularly for mammography. This phenomenon can be observed at a macrolevel: those regions with higher uptake are also those with higher access in the frameworks of screening programmes or of the NHS. The effect on total uptake

of organized screening with active invitations to the target population is well known and has been observed in all contexts.[23,11,24] Finally, it is also interesting to note that total and screening programme uptake patterns are similar in almost all regions. This suggests that where the population's attention to prevention is low, there has also been difficulty in implementing screening programmes. This result is consistent with the consolidated evidence of an association between low/changeable invitation coverage of screening programmes and low response from the population to invitations.[5,6,20,21]

It is not easy to understand the causal relationship; if a context is unfavourable to the organisation of complex and multidisciplinary paths, is this because the population in that context does not trust the NHS and thus does not respond to the invitation? Or is it because the poor organisation directly penalises compliance with programme recommendations?

Socioeconomic differences

Socioeconomic differences in uptake are still very evident, whichever variable is considered: education, citizenship, occupation or perceived economic difficulties. In particular, foreign women had a 40% lower uptake probability than Italians for Pap test and 55% lower probability for mammography. In Italy, immigration is a recent phenomenon, with a marked increase during the first decade of the 2000s, so it is conceivable that both cultural and language barriers may influence access to screening programmes and health services. However, a recent paper showed that screening uptake was heterogeneous by area of origin (Africans have lower Pap test and mammography uptake) and by region of residence,[25] highlighting that there are margins for improving equity. Regarding education, our result confirms what has been observed in England,[26] where a recent study showed a significant improvement of equitable delivery of breast screening but not of cervical screening.[27] Unfortunately, our dataset did not include information on income, though we can show the effect of economic conditions indirectly through survey respondents' perceived economic difficulties. Nevertheless, its association with uptake is more difficult to interpret, as this variable combines objective available resources and factors related to more subjective perception of precarious conditions or worsening of one's economic situation.[11] These latter factors are more related to personal coping - the ability to react to changes and difficulties, a personal characteristic known to be associated with participation in screening; "maladaptive coping", instead, is associated with poor compliance with cancer screening recommendations.[16] These personal characteristics are difficult to modify through active interventions such as invitation letters or information campaigns.[11,28]

Even though organized screening programmes and the NHS guarantee wider and easier access to screening, thus increasing coverage in all contexts, surprisingly, no reduction in socioeconomic differences was observed in the areas where screening programmes had higher invitation coverage. This effect on reducing access inequalities has been observed in other Italian studies.[13,29] Furthermore, the implementation of screening programmes has shown a levelling effect on breast cancer outcomes, with women in the lowest socioeconomic level attaining the same survival rates as those in the highest socioeconomic level.[30,31]A decrease in inequalities in access to effective prevention measures thanks to screening programmes and to the NHS actively promoting interventions has been observed in a number of other studies,[6,11,32,33] even though considerable exceptions or failures have also been observed.[34,35,36]

Association with other preventive health behaviours

We observed associations between screening uptake and single preventive health behaviours in organised programs and in public in private opportunistic setting. The existing synergy between prevention interventions and preventive health behaviours is a well-known phenomenon which offers the NHS opportunities to promote coordinated prevention initiatives.[37]

The association between both screening test uptake and being a former smoker is not surprising and has been reported by other authors;[38,39] instead, a slightly higher uptake for both Pap test and mammography in current smokers than in non-smokers is more surprising. It should be noted that, in women, the prevalence of smoking in Italy is higher among the highly educated; the difference in screening uptake thus almost disappears when adjusting for educational level. Particular attention should be paid to the association between mammography uptake and use of CAM, a partially unexpected result, as breast screening has been criticized in the last few years by groups concerned with overdiagnosis and overtreatment and against the medicalisation of the healthy population.[40,41] These opinions, which are not against technology per se, are welcome in cultural contexts that refuse a technological approach to life and health care and that are often attracted to CAM.[42] A positive association between CAM and mammography coverage thus suggests that a lack of coverage is, to a large degree, not a conscious choice but instead due to the lack of access to the service.

Limitations and strengths of the study and comparison with other data

The main limitations of the data used in the present study are related to data collection techniques, namely a retrospective study based on the recall of the interviewed women. When recalling past events, it can be difficult to distinguish between different organizational and administrative ways of

how the test was delivered. For example, a test undergone in the framework of a screening programme could be confused with a test provided by the NHS outside an organised programme (in some local health services, the patient cannot perceive this difference). This observation does not influence total uptake but can generate incorrect classification of access modalities that can differ between Italian women and foreign nationals or between different educational levels. In fact, it can be difficult to define just what a "screening programme" is, resulting in a possible misunderstanding and thus confusing it with a more general access to a public health centre, particularly by less educated women or foreigner nationals with linguistic barriers. For this reason, most of the analysis was conducted by using the two indicators "public sector uptake" and "screening programme uptake" to give an idea of the range of the actual data. Furthermore, some women undergo tests at shorter intervals than is recommended,[6,43] which can mask part of the uptake obtained by the NHS when we look at the most recent test only, as in this survey. In fact, if a woman has already undergone a test performed in the NHS and then undergoes an opportunistic test before the recommended interval has expired, she will register as covered by the opportunistic test and not by the previous NHS test. Thus, we underestimate the coverage by the public sector, which adopts less intensive protocols and longer intervals.[43,,44] Furthermore, a survey with less stringent questions to identify the date of the last screening test may overestimate coverage due to telescoping effect (women reporting having undergone the test more recently than in fact they have), as noted in a previous Italian survey.[44] Indeed, the questions about the last screening test are posed slightly differently in the Italian NHIS and in the routine surveillance system – the PASSI survey – managed by the local health authorities.[34] This surveillance reports an overall uptake of 77% and 70% for cervical and breast cancer screening, respectively. It is also important to underline that the HPV test, which was authorized as a primary screening test instead of the Pap test in women older than 30-35 years in January 2013 by the Italian Ministry of Health, was available only through some pilot projects until 2014. Given that the NHIS interviews were conducted in 2012-2013 and that the questions referred to tests undergone in the three preceding years, obviously very few women had been invited to HPV screening at that point.[20,29,44] Among the strengths of this study to be mentioned is the enormous information potential of the Istat survey, both at the individual and at the family level, offering a very rich description of individual women, their families and their socioeconomic status. Unfortunately, for this study, we had access to a restricted dataset of the NHIS. Therefore the association between screening uptake and some potentially relevant information, as the family composition or the citizenship of the partner, could not be studied.

Another strong point is the inclusion of an ecological variable on the screening offered from a second data source. The joint use of these two data sources made it possible to estimate the impact

of screening programmes on overall screening uptake and on differences in screening uptake between regions taking into account different socioeconomic and behavioural characteristics.

Conclusions

Total coverage observed through the Italian NHIS is below the desired and acceptable levels recommended by the European Commission.

Screening programmes increase uptake and have the potential, when correctly implemented, to decrease geographical inequalities, although not those differences caused by individual attitudes towards health and prevention.

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Contributors

AP, PGR and LG designed and initiated the study and wrote the manuscript. LF extracted the data, conducted statistical analysis, interpreted the findings and reviewed/edited the manuscript. BG conducted statistical analysis. ADN reviewed and edited the manuscript. MZ and CM contributed to the discussion and critically reviewed the final manuscript. All authors read and approved the final manuscript.

Data sharing statement

The analyses were performed using data based on Istat's surveys. In particular, we used Istat's standard files (issued upon request with a valid reason for research purposes and released free of charge and in compliance with the principle of statistical secrecy and protection of personal data). To acquire such files, it is necessary to register in the area of the Istat website dedicated to data use and to accept the terms of use. Data are available in different formats (TXT, STATA, SAS, R).

Competing interests

None declared

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References

1. Osservatorio Nazionale Screening. 2014. I programmi di screening in Italia. http://www.osservatorionazionalescreening.it/sites/default/files/allegati/Screening_2014_web.pdf
2. Giorgi D, Giordano L, Ventura L, et al. Mammography breast cancer screening in Italy: 2010 survey. *Epidemiol Prev* 2012;361:8–27.
3. von Karsa L, Anttila A, Ronco G, et al., eds. Cancer screening in the European Union. Report on the implementation of the Council Recommendation on cancer screening. First report. Luxembourg: European Commission, 2008.
4. Perry N, Broeders M, de Wolf C, et al., eds. European guidelines for quality assurance in breast cancer screening and diagnosis. Luxembourg: European Commission. Office for Official Publications of the European Communities, 2006.
5. Zappa M, Carozzi FM, Giordano L, et al. The diffusion of screening programmes in Italy, years 2011-2012. *Epidemiol Prev* 2015;39:5–8.
6. Giorgi Rossi P, Camilloni L, Cogo C, et al. [Methods to increase participation in cancer screening programmes]. *Epidemiol Prev* 2012;36:1–104.
7. ISTAT. La prevenzione dei tumori femminili in Italia il ricorso a Pap test e mammografia. Anni 2004-2005. Roma, 2006.
8. Giorgi Rossi P, Carrozzi G, Federici A, et al. Invitation coverage and participation in Italian cervical, breast and colorectal cancer screening programmes. *J Med Screen* 2017;Jan1. doi: 10.1177/0969141317704476.
9. Green LW and Kreuter MW. Health program planning: an educational and ecological approach. 4th ed. New York: McGraw-Hill, 2005.
10. Federici A, Guarino A, Serantoni G. Adesione ai programmi di screening di prevenzione oncologica: proposta di una modellizzazione dei risultati di revisione della letteratura secondo il Modello PRECEDE-PROCEED. *Epidemiol Prev* 2012;36:1–104.
11. Palència L, Espelt A, Rodríguez-Sanz M, et al. Socio-economic inequalities in breast and cervical cancer screening practices in Europe: influence of the type of screening program. *Int J Epidemiol* 2010;39:757–65. doi: 10.1093/ije/dyq003.
12. Jepson R, Clegg A, Forbes C, Lewis R, Sowden A, Kleijnen J. The determinants of screening uptake and interventions for increasing uptake: a systematic review. Health Technol Assess. 2000;4(14):i-vii, 1-133.
13. Labeit, A., Peinemann, F., Baker, R., 2013. Utilisation of preventative health check-ups in the UK: findings from individual-level repeated cross-sectional data from 1992 to 2008. BMJ Open 3, e003387. doi:10.1136/bmjopen-2013-003387

14. Zappa, M., Castiglione, G., Giorgi, D., Grazzini, G., Paci, E., Ciatto, S., 1998. Re: Participation in colorectal cancer screening: a review. J. Natl. Cancer Inst. 90, 465.
15. Wools, A., Dapper, E.A., Leeuw, J.R.J. de, 2016. Colorectal cancer screening participation: a systematic review. Eur. J. Public Health 26, 158–168. doi:10.1093/eurpub/ckv148
16. Douglas E, Waller J, Duffy SW, Wardle J. Socioeconomic inequalities in breast and cervical screening coverage in England: are we closing the gap? J Med Screen. 2016 Jun;23(2):98-103. doi: 10.1177/0969141315600192.
17. ISTAT. 2006. Fattori di rischio e tutela della salute — Indagine multiscopo sulle famiglie italiane "Prevenzione dei tumori femminili: ricorso a pap test e mammografia" anni 2004/2005. http://www3.istat.it/salastampa/comunicati/non_calendario/20061204_00/testointegrale.pdf
18. ISTAT. 2013. Multiscopo sulle famiglie: condizioni di salute e ricorso ai servizi sanitari. http://siqual.istat.it/SIQual/visualizza.do?id=0071201
19. Ronco G, Giorgi Rossi P, Giubilato P, et al. A first survey of HPV-based screening in routine cervical cancer screening in Italy. *Epidemiol Prev* 2015;39:77–83.
20. Ronco G, Giubilato P, Carozzi F, et al. Extension of organized cervical cancer screening programmes in Italy and their process indicators, 2011-2012 activity. *Epidemiol Prev* 2015;39:61–76.
21. Ventura L, Giorgi D, Giordano L, et al. Mammographic breast cancer screening in Italy: 2011-2012 survey. *Epidemiol Prev* 2015;39:21–9.
22. Anttila A, Ronco G, Nicula F, et al. Organization of cytology-based and HPV-based cervical cancer screening. In: Anttila A, Arbyn M, De Vuyst H, et al., eds. European guidelines for quality assurance in cervical cancer screening. Luxembourg: Publications Office of the European Union, 2015, Second edition – supplements: pp. 69–108.
23. Nygård JF, Skare GB, Thoresen SØ. The cervical cancer screening programme in Norway, 1992-2000: changes in Pap smear coverage and incidence of cervical cancer. *Med Screen* 2002;9(2):86-91.
24. Ferroni E, Camilloni L, Jimenez B, et al. How to increase uptake in oncologic screening: a systematic review of studies comparing population-based screening programs and spontaneous access. *Prev Med* 2012;55:587–96. doi: 10.1016/j.ypmed.2012.10.007.
25. Francovich L, Di Napoli A, Giorgi Rossi P, Gargiulo L, Giordani B, Petrelli A. [Cervical and breast cancer screening among immigrant women resident in Italy]. Epidemiol Prev. 2017 May-Aug;41(3-4 (Suppl 1)):18-25. doi: 10.19191/EP17.3-4S1.P018.061. Italian.
26. Sabates R, Feinstein L. The role of education in the uptake of preventative health care: the case of cervical screening in Britain. Soc Sci Med. 2006 Jun;62(12):2998-3010.

27. Sabates R, Feinstein L. Do income effects mask social and behavioural factors when looking at universal health care provision? Int J Public Health. 2008;53(1):23-30. PubMed PMID: 18522366.
28. Federici A, Poletti P, Guarino A, et al. Garantire la partecipazione consapevole. In: Federici A, ed. Screening - Profilo complesso di assistenza. Roma: Il Pensiero Scientifico, 2007: pp. 252–257.
29. Carrozzi G, Sampaolo L, Bolognesi L, et al. Cancer screening uptake: association with individual characteristics, geographic distribution, and time trends in Italy. *Epidemiol Prev* 2015;39:9–18.
30. Pacelli B, Carretta E, Spadea T, et al. Does breast cancer screening level health inequalities out? A population-based study in an Italian region. *Eur J Public Health* 2014;24:280–5. doi: 10.1093/eurpub/ckt119.
31. Puliti D, Miccinesi G, Manneschi G, et al. Does an organised screening programme reduce the inequalities in breast cancer survival? *Ann Oncol* 2012;23:319–23. doi: 10.1093/annonc/mdr121.
32. Spadea T, Bellini S, Kunst A, et al. The impact of interventions to improve attendance in female cancer screening among lower socioeconomic groups: a review. *Prev Med* 2010;50:159–64. doi: 10.1016/j.ypmed.2010.01.007.
33. Giorgi Rossi P, Baldacchini F, Ronco G. The Possible Effects on Socio-Economic Inequalities of Introducing HPV Testing as Primary Test in Cervical Cancer Screening Programs. *Front Oncol* 2014;4:20. doi: 10.3389/fonc.2014.00020.
34. Lagerlund M, Bellocco R, Karlsson P, et al. Socio-economic factors and breast cancer survival - a population-based cohort study (Sweden). *Cancer Causes Control* 2005;16:419–30.
35. Louwman WJ, van de Poll-Franse LV, Fracheboud J, et al. Impact of a programme of mass mammography screening for breast cancer on socio-economic variation in survival: a population-based study. *Breast Cancer Res Treat* 2007;105:369–75.
36. Halmin M, Bellocco R, Lagerlund M, et al. Long-term inequalities in breast cancer survival--a ten year follow-up study of patients managed within a National Health Care System (Sweden). Acta Oncol 2008;47:216–224. doi: 10.1080/02841860701769768.
37. Bankhead CR, Brett J, Bukach C, et al. The impact of screening on future health-promoting behaviours and health beliefs: a systematic review. *Health Technol Assess* 2003;7:1–92.
38. Venkataraman K, Wee HL, Ng SHX, *et al.* Determinants of individuals' participation in integrated chronic disease screening in Singapore. *J Epidemiol Community Health* 2016;70:1242–50. doi:10.1136/jech-2016-207404

39. Labeit A, Peinemann F, Baker R. Utilisation of preventative health check-ups in the UK: findings from individual-level repeated cross-sectional data from 1992 to 2008. *BMJ Open* 2013;3:e003387. doi:10.1136/bmjopen-2013-003387
40. Grady D. Look for cancer, and find it! In: New York Times, 2014. http://well.blogs.nytimes.com/2014/04/07/look-for-cancer-and-find-it/
41. Gøtzsche PC, Hartling OJ, Nielsen M, Brodersen J, Jørgensen KJ. Breast screening: the facts--or maybe not. BMJ 2009;338:b86–b86. doi: 10.1136/bmj.b86.
42. Volpi R. L'amara medicina. Come la sanità italiana ha sbagliato strada. Milano: Feltrinelli, 2008.
43. Ronco G, Segnan N, Giordano L, et al. Interaction of spontaneous and organised screening for cervical cancer in Turin, Italy. *Eur J Cancer* 1997;33:1262–7.
44. Giorgi Rossi P, Esposito G, Brezzi S, et al. Estimation of Pap-test coverage in an area with an organised screening program: challenges for survey methods. *BMC Health Serv Res* 2006;6:36.

Box 1. Characteristics of the Italian organized screening programmes in 2013.

	Cervical cancer screening	Breast Cancer Screening
Target age	25-64	50-69 [a]
Test	Pap test [b]	Mammography (double projection)
Interval	3 years	2 years
Proportion of the target population regularly invited	70.8%	73.9%
Participation rate	40.9%	57.0%

[a] In two regions, Emilia-Romagna and Piedmont, the target age was extended in 2010 to ages 45-74. In these regions the screening interval is one year for women aged 45-49.

[b] Since January 2013, the Italian Ministry of Health now recommends HPV-DNA test, followed by cytology triage in case of HPV positivity, with 5-year interval, as an alternative option to Pap test every three years for women >=30. When the interviews was conducted in 2013, only few pilot studies used HPV as primary screening test, accounting for 7.5% and 6.9% of the invited population in 2012 and 2013, respectively.

Table 1. Pap test and mammography: total uptake, uptake in the National Health Service and public screening coverage, by educational level, occupation, and perception of economic family resources. Italy, 2012-2013.

	PAP TEST (n=32,831)			MAMMOGRAPHY (n=16,459)		
		uptake in the NHS			uptake in the NHS	
	Total uptake	Of which public screening coverage	Total	Total uptake	Of which public screening coverage	Total
Age						
25-29	48.5	13.3	28.2			
30-34	58.1	18.6	35.7			
35-39	63.8	19. 9	37.3			
40-44	65.1	21.9	38.2			
45-49	72.1	23.6	42.8			
50-54	69.1	26.6	45.2	60.5	28.1	44.9
55-59	60.2	25.9	41.4	57.7	29.8	44.4
60-64	53.3	25.7	39.1	55.4	32.2	44.8
65-69				50.7	29.4	41.6
Citizenship						
Italian	63.2	26,0	37.4*	55.9	30.7	44.2
Foreign national	52.2	23.8	40.6	41.4	20.9	32.4
Educational level						
Degree	68.6	20.2	37.2	65.5	29.9*	46.5
School-leaving certificate	64.6	21.5	37.4	60.8	28.8	44.3
Compulsory education	57.8	23.6	40.8	53.3	30.2	43.5
Occupation						
Executive, Entrepreneur, Freelance professional	74.4	20.1	35.4	65.1	27.8	40.9
Office worker	73,0	23.9	40.4	68.1	33.1	49.7
Workman, Apprentice, Other	64.1	28.2	45.8	58.2	34.6	48.6
Independent businessman, Homecare assistant, Cooperative member	67.5	24.7	40.2	60.5	35.7	50.4
Contract worker	60.2	20.3	34.4	59.9	21.3	40.4
Not employed	54.1	19.5	36.3	52.8	28.3	41.9
Perceived economic resources						
Excellent/Adequate	66.0	25.6	41.8	60.9	32.4	46.9
Scarce/Insufficient	53.9	21.9	38.8	48.6	25.4	39.2
Reasons hampering pursuit of hobbies or interests						
Other	60.3	22.0	38.7	55.4	29.5	43.3
Too busy	67.6	22.9	39.5	61.1	31.3	47.7
Smoking habits						
Smoker	62.2	21.9	38.6	56.6	30.9	45,0
Former smoker	70.9	26.8	43.8	63.8	35.2	51.3
Non-smoker	59.6	21.1	37.6	53.8	27.7	41.3
Physical activity						
No	55.9	19.4	36.2	47.7	24,0	37.3

Yes	67.9	24.8	41.4	64.9	35.5	50.6
Weight control						
Rarely or never	56.9	20.7	36.1	48.7	25.2	37.7
Weight controlled	65.2	23.1	40.6	61.4	32.9	48.2
Preventive medical examinations in the preceding 4 weeks						
No examination	58.0	20.9	37,0	52.2	28.2	41,0
At least one preventive examination	75.0	23.7	41.8	65.8	32.9	49.5
Examinations for other reasons	68.7	25.5	43.4	61.8	32.1	48.5
General prevention medical tests						
No test	43.7	16,0	28.5	35,0	18.9	27.2
1 or 2 tests	56.9	22.2	37.5	50.2	31.3	42.5
All tests	64.7	23,0	40.3	57.5	30.2	44.8
Use of complementary and alternative medicine						
Never used or more than three years ago	60.0	21.3	38.2	54.9	29.1	43,0
At least once in the last three years	79.2	29.6	44.8	68.5	35.9	52.2
Total	**62.1**	**22.2**	**38.9**	**56.4**	**29.8**	**44,0**

All differences are statistically significant, except *

Table 2. Multilevel logistic random intercept model for Pap test. Model on having had the test in the three years prior to interview. Italy, 2012-2013.

Variable		Adjusted OR	95% CI	
Individual				
Age group	25-34	1		
	35-44	1.45	1.33	1.56
	45-54	1.89	1.75	2.04
	55-64	0.99	0.92	1.08
Citizenship	Foreign national	1		
	Italian	1.69	1.54	1.85
Educational level	Compulsory education	1		
	School-leaving certificate	1.12	1.05	1.19
	Degree	1.16	1.08	1.27
Perceived economic resources	Scarce, Absolutely insufficient	1		
	Excellent, adequate	1.25	1.18	1.32
Occupation	Unemployed	1		
	Executive, Entrepreneur, Freelance professional	1.08	0.87	1.32
	Office worker	1.35	1.16	1.54
	Workman, Apprentice, Other	1.18	1.05	1.32
	Independent businessman, Homecare assistant, Cooperative member	1.15	1.06	1.23
	Contract worker	1.28	1.19	1.37
Reasons hampering pursuit of hobbies or interests	Other reasons	1		
	Too busy	1.19	1.12	1.27
Smoking habits	Non-smoker	1		
	Former smoker	1.37	1.28	1.45
	Smoker	1.08	1.01	1.15
Physical activity	No	1		
	Yes	1.16	1.10	1.22
Weight control	Rarely or never	1		
	Periodically	1.25	1.19	1.32
Preventive medical examinations in the preceding 4 weeks	No examination	1		
	Other reasons	1.43	1.33	1.52
	Preventive examination	1.75	1.59	1.92
General prevention medical tests	No test	1		
	1 or 2 tests	1.41	1.25	1.61

	All tests	1.85	1.72	2.00
Use of complementary and alternative medicine	Never used or more than three years ago	1		
	At least once in the last three years	1.41	1.30	1.54
Contextual				
Invitation coverage in the period 2011-13	Within the median	1		
	above the median	2.12	1.43	3.13
Random effect				
		Estimate	**Standard error**	**P-value**
$\alpha_{i,\ regions}$		0.209	0.066	<0.01
ICC - Intraclass Correlation Coefficient (ρ)		0.06		

Table 3. Multilevel logistic random intercept model for mammography. Model on having had mammography in the two years before interview. Italy, 2012-2013.

Variable		Adjusted OR	95% CI	
Individual				
Age group	50-59	1		
	60-69	0.75	0.69	0.81
Citizenship	Foreign national	1		
	Italian	2.22	1.85	2.70
Educational level	Compulsory education	1		
	School-leaving certificate	1.09	0.99	1.18
	Degree	1.30	1.14	1.47
Perceived economic resources	Scarce, Absolutely insufficient	1		
	Excellent, adequate	1.23	1.15	1.33
Occupation	Unemployed	1		
	Executive, Entrepreneur, Freelance professional	1.47	0.94	2.27
	Office worker	0.99	0.79	1.25
	Workman, Apprentice, Other	1.02	0.86	1.20
	Independent businessman, Homecare assistant, Cooperative member	1.10	0.97	1.25
	Contract worker	1.23	1.10	1.37
Reasons hampering pursuit of hobbies or interests	Other reasons	1		
	Too busy	1.15	1.04	1.25
Smoking habits	Non-smoker	1		
	Former smoker	1.18	1.09	1.28
	Smoker	1.00	0.92	1.10
Physical activity	No	1		
	Yes	1.37	1.28	1.47
Weight control	Rarely or never	1		
	Periodically	1.33	1.25	1.43
Preventive medical examinations in the last 4 weeks	No examination	1		
	Other reasons	1.52	1.41	1.64
	Preventive examination	1.56	1.41	1.75
General prevention medical tests	No test	1		
	1 or 2 tests	1.43	1.12	1.82
	All tests	2.00	1.69	2.38

Use of complementary and alternative medicine	Never used or more than three years ago	1		
	At least once in the last three years	1.22	1.09	1.37
Contextual				
Invitation coverage in the period 2011-13	Within the median	1		
	Above the median	2.00	1.43	2.78
Random effect				
		Estimate	**Standard error**	**P-value**
$\alpha_{i,\ regions}$		0.136	0.045	<0.01
ICC- Intraclass Correlation Coefficient (ρ)		0.04		

Figure legends

Figure 1. Utilization of Pap test (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

Figure 2. Utilization of Pap test (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

Figure 3. Utilization of mammography (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

Figure 4. Utilization of mammography (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

Figure 5. Level 2 residuals of hierarchical models for Pap test and mammography. Italy, 2012-2013.

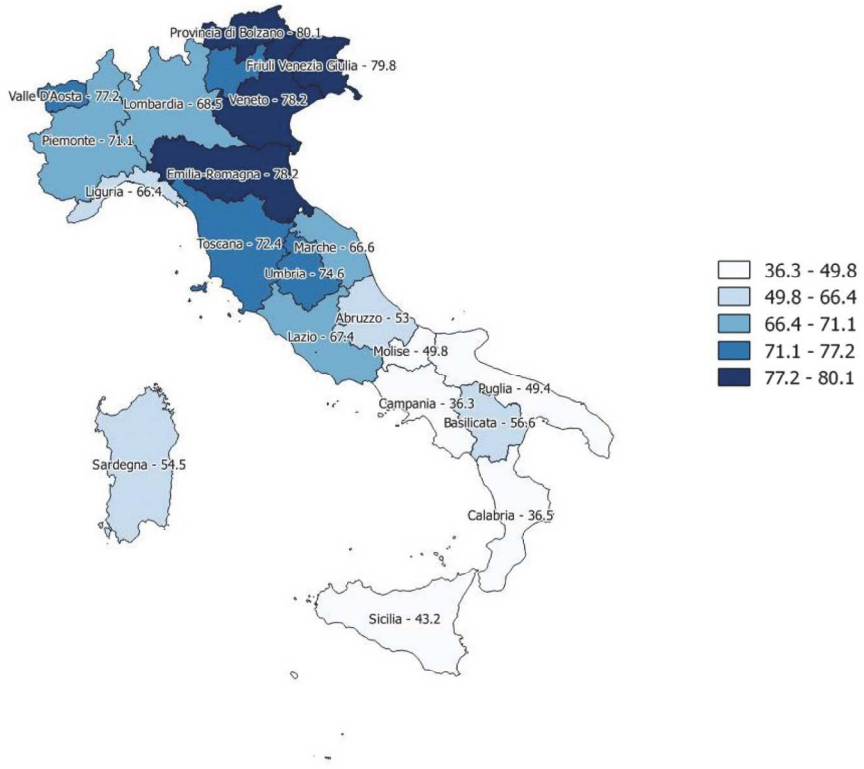

Figure 1. Utilization of Pap test (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

160x126mm (300 x 300 DPI)

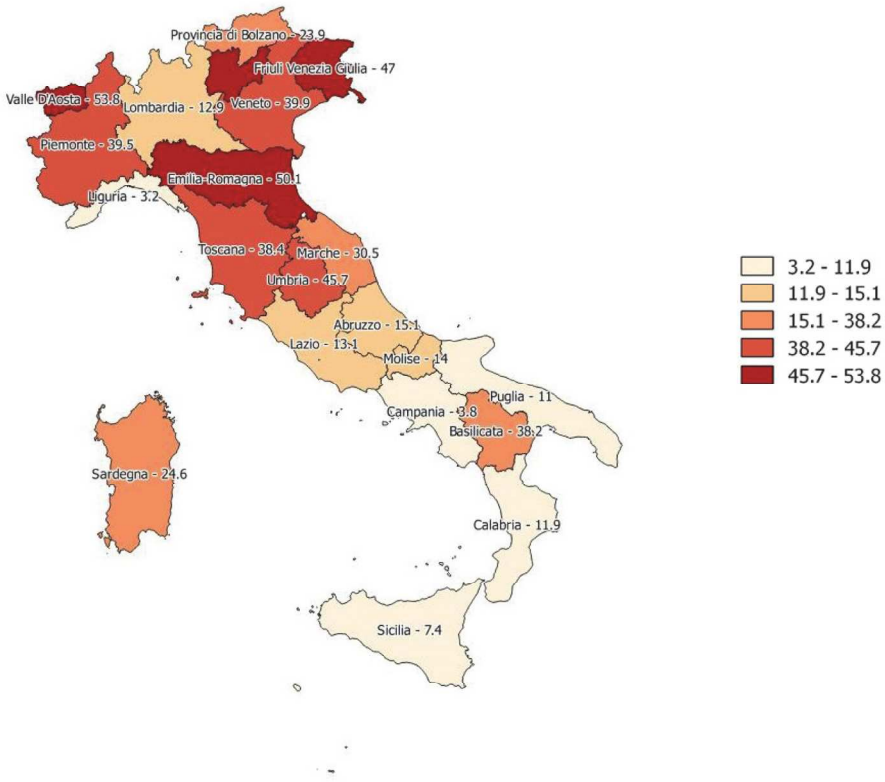

Figure 2. Utilization of Pap test (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

157x125mm (300 x 300 DPI)

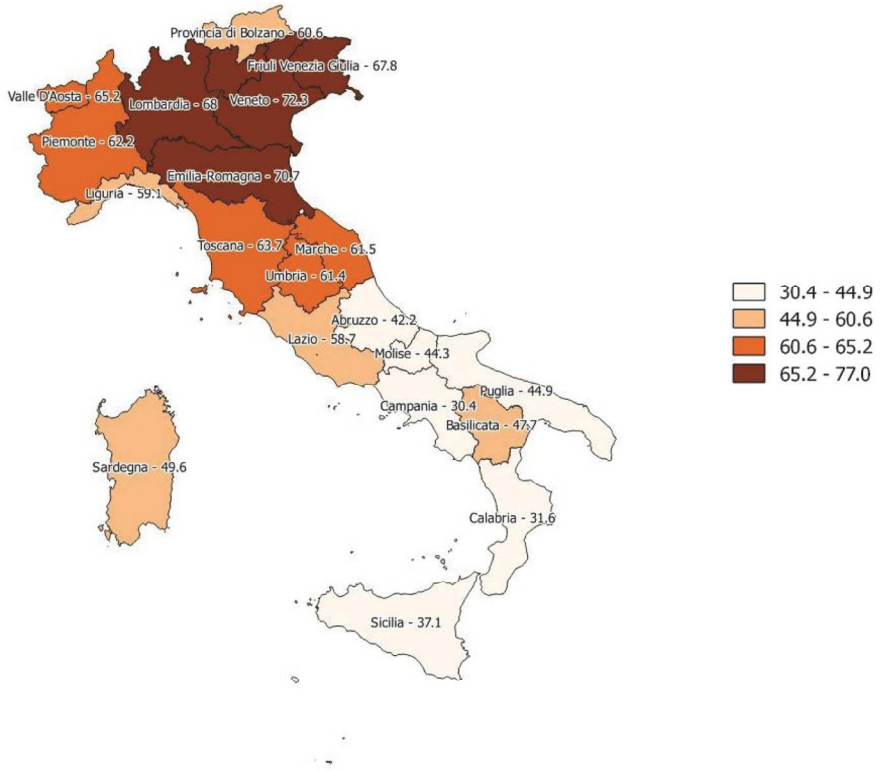

Figure 3. Utilization of mammography (* 100 women in the target group). Total test uptake with the recommended schedule. Italy, 2012-2013.

159x124mm (300 x 300 DPI)

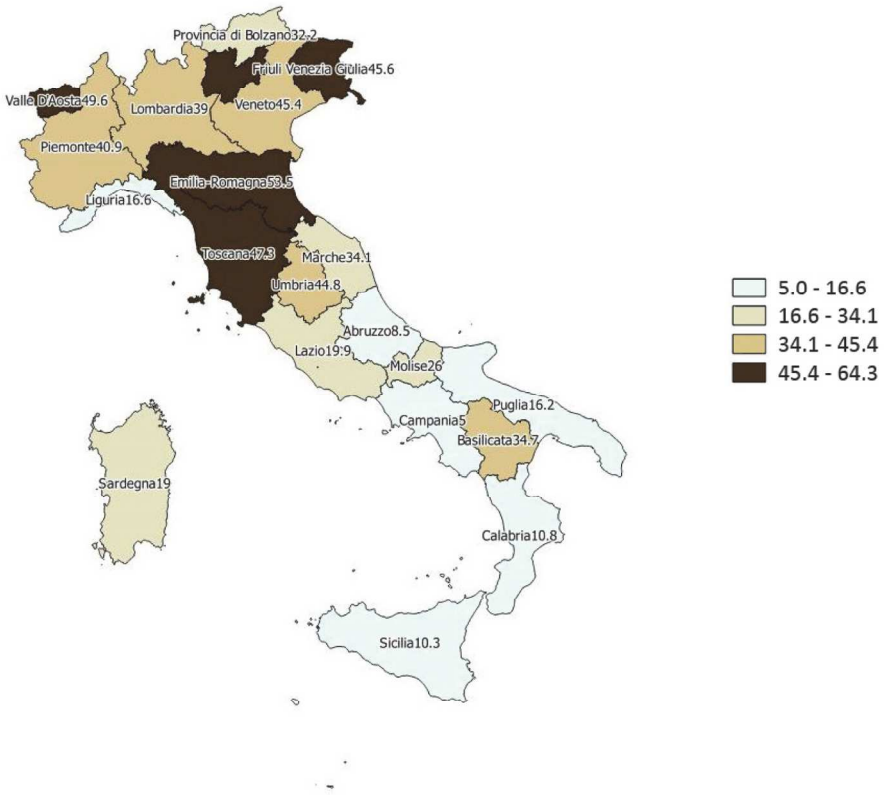

Figure 4. Utilization of mammography (* 100 women in the target group) within organised public screening programme. Italy, 2012-2013.

154x125mm (300 x 300 DPI)

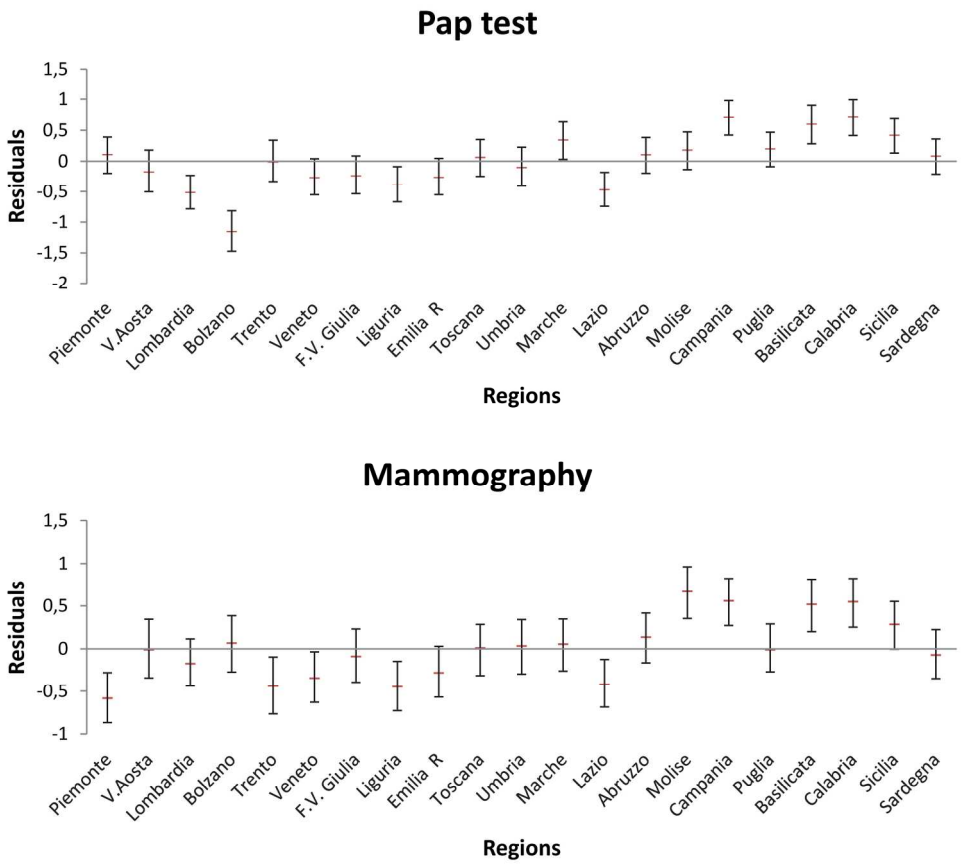

Figure 5. Level 2 residuals of hierarchical models for Pap test and mammography. Italy, 2012-2013.

175x158mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods	

taking account of sampling strategy

(*e*) Describe any sensitivity analyses

Continued on next page

Results			**Page number**
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	6-7
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-8
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.